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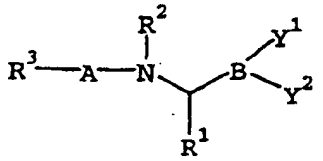
(54) Title: PEPTIDE BORONIC ACID INHIBITORS OF HEPATITIS C VIRUS PROTEASE



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(57) Abstract: The present invention relates generally to novel α-aminoboronic acids and corresponding peptide analogs represented by structural Formula (I) or pharmaceutically acceptable salt forms thereof, wherein R^1, R^2, R^3, Y^1, Y^2, and A are described herein. The invention is also concerned with pharmaceutical formulations comprising these novel compounds as active ingredients and the use of the novel compounds and their formulations in the treatment of hepatitis C viral infections. The compounds of the invention are inhibitors of hepatitis C viral protease.

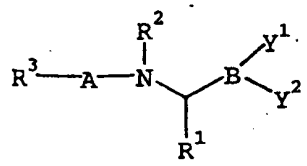
WO 01/02424 A2

TITLE

PEPTIDE BORONIC ACID INHIBITORS OF HEPATITIS C VIRUS PROTEASE

FIELD OF THE INVENTION

The present invention relates generally to novel α-aminoboronic acids and corresponding peptide analogs represented by structural Formula (I):



(I)

or phamaceutically acceptable salt forms thereof, wherein R^1, R^2, R^3, Y^1, Y^2, and A are described herein. The invention is also concerned with pharmaceutical formulations comprising these novel compounds as active ingredients and the use of the novel compounds and their formulations in the treatment of hepatitis C viral infections. The compounds of the invention are inhibitors of hepatitis C viral protease.

BACKGROUND

Hepatitis C virus (HCV) is the major cause of transfusion and community-acquired non-A, non-B hepatitis worldwide. Approximately 2% of the world's population are infected with the virus. In the Unites States, hepatitis C represents approximately 20% of cases of acute hepatitis. Unfortunately, self-limited hepatitis is not the most common course of acute HCV infection. In the majority of patients, symptoms of acute hepatitis resolve, but ALT levels (a liver enzyme diagnostic for liver damage) often remain elevated and HCV RNA persists. Indeed, a propensity to chronicity is the most distinguishing characteristic of hepatitis C, occurring in at least 85% of patients with acute HCV infection. The factors that lead to chronicity

in hepatitis C are not well defined. Chronic HCV infection is associated with increased incidence of liver cirrhosis and liver cancer. No vaccines are available for this virus, and current treatments are largely restricted to the use of alpha interferon, which is effective in less than 1/3 of patients. HCV is a positive-stranded RNA virus. Based on comparison of deduced amino acid sequence and the extensive similarity in the 5' untranslated region, HCV has been classified as a separate genus in the Flaviviridae family, which also includes flaviviruses (such as yellow fever virus (YF)), and animal pestiviruses (like bovine viral diarrhea virus (BVDV) and swine fever virus (CSFV)). All members of the Flaviviridae family have enveloped virions that contain a positive stranded RNA genome encoding all known virus-specific proteins via translation of a single, long uninterrupted, open reading frame.

Considerable heterogeneity is found within the nucleotide and encoded amino acid sequence throughout the HCV genome. At least 6 major genotypes have been characterized, and more than 50 subtypes have been described. The major genotypes of HCV differ in their distribution worldwide; the clinical significance of the genetic heterogeneity of HCV remains elusive despite numerous studies of the possible effect of genotypes on pathogenesis and therapy.

The RNA genome is about 9.6 Kb in length, and encodes a single polypeptide of about 3000 amino acids. Within the genomic organization the 5' and 3' ends are of critical importance for the replicative life cycle. The 5' end contains an Internal Ribosome Entry Site or IRES, which directs cellular ribosomes to the correct AUG for initiation of translation. As was determined by transient expression of cloned HCV cDNAs, the precursor protein is cotranslationally and posttranslationally processed into at least 10 viral structural and nonstructural proteins by the action of a host signal peptidase and by two distinct viral proteinase activities. The translated product contains the

following proteins: core-E1-E2-p7-NS2-NS3-NS4A-NS4B-NS5A-NS5B.

The N-terminal portion of NS3 functions as a proteolytic enzyme that is responsible for the cleavage of sites liberating the nonstructural proteins NS4A, NS4B, etc. Agents that block this protease are expected to be new antiviral agents. This protease has been classified as a "serine protease" based on the catalytic residues in the active site, Eckart et al. *Biochem. Biophys. Res. Commun.* 192, 399-406 (1993). It is known in the art that peptide analogs corresponding to sequences of peptide substrate and containing an electrophilic group provide good inhibitors of serine proteases. Enzyme susceptibility to inhibition differs significantly by choice of the electrophilic group. In the present invention, inhibitors of HCV protease corresponding to the sequence of the NS5A/B cleavage site have been prepared with an electrophilic boronic acid group incorporated into the sequence.

Boronic acids have a distinct advantage over other peptide inhibitors of HCV protease. The concept of using boronic acids as serine protease inhibitors was introduced in the early 70's Antonov et al. *FEBS Lett* 7, 23 (1970); Koelhler and Lienhard *Biochemistry* 10, 2477-2483 (1971). An α-amino-boronic acid, Ac-boroPhe-OH, was first prepared by Matteson *J. Am. Chem. Soc.* 103, 5241-5242 (1981). This compound inhibits chymotrypsin with a K_i of 2.1 μM. Kettner and Shenvi *J. Biol. Chem.* 259, 15106-15114 (1984) were able to couple α-amino-boronic acids to peptides and were able to show that such compounds were very effective inhibitors of the serine proteases, leukocyte elastase, pancreatic elastase, cathepsin G, and chymotrypsin. However, the specificity of the α-aminoboronic acid for enzyme inhibition was highly dependent on the nature of the side chain. Examples of di, tri and tetra peptides where the α-aminoboronic acid is a boroLeu, boroVal, boroPhe, boroAla or boroIle, are described by Shenvi et al. in US 4,499,082.

More recent patents cover peptide boronic acids containing basic side chains. Kettner et al. in US 5,187,157 discloses boronic acid inhibitors specially designed as inhibitors of trypsin-like serine proteases such as thrombin, plasma kallikrein and plasmin, wherein the α-aminoboronic acid side chain is an aklyl group substituted by $-NH_2$, $-NH-C(NH)-NH_2$ or $-S-C(NH)-NH_2$.

In US 5,462,964, Fevig et al. disclose boronic acid dipeptide inhibitors which are inhibitors of trypsin-like serine proteases wherein the α-aminoboronic acid side chain is a substituted alkyl or substituted alkylphenyl group.

In US 5,658,885, Lee et al. disclose boronic acid peptide inhibitors which are inhibitors of thrombosis and anticoagulants wherein the α-aminoboronic acid side chain is an aklyl, substituted alkyl, substituted phenylaklyl, or substituted cycloalkylalkyl group.

In US 5,639,739, Dominques et al. disclose boronic acid peptide inhibitors which are inhibitors of trypsin-like serine proteases wherein the α-aminoboronic acid side chain is functionalized imidazole containing alkyl group.

In US 5,698,538, Amparo et al. disclose boronic acid inhibitors which are thrombin inhibitors wherein the α-aminoboronic acid side chain is a monosubstituted alkyl, monosubstituted alkenyl, or a monosubstituted phenylalkyl group.

In US 5,866,684, Attwood et al., as well as WO 98/22496, hexapeptide boronic acid inhibitors are disclosed which are HCV protease inhibitors wherein the α-aminoboronic acid side chain is an alkyl or an alkenyl group.

Even with the current knowledge of α-aminoboronic acid compounds as inhibitors of serine proteases, it is still desirable to develop more efficacious inhibitors which are enzyme specific to HCV protease. The present invention discloses α-aminoboronic acid compounds as efficacious inhibitors of the NS3 protease of the hepatitis C virus.

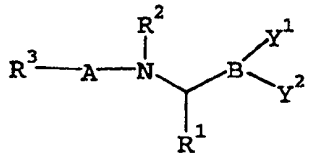
SUMMARY OF THE INVENTION

One object of the presenbt invention is to provide compounds, or pharmaceutically acceptable salt forms or prodrugs thereof, which are useful as inhibitors of hepatitis C virus protease, more specifically, the NS3 protease.

It is another object of the present invention to provide pharmaceutical compositions comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound of Formula (I), or pharmaceutically acceptable salt form or prodrug thereof.

It is another object of the present invention to provide a method for the treatment or prevention of HCV comprising administering to a host in need of such treatment a therapeutically effective amount of a compound of Formula (I), or a pharmaceutically acceptable salt form or prodrug thereof.

These and other objects of the invention, which will become apparent during the following detailed description, have been achieved by the discovery that compounds of Formula (I)



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Or pharmaceutically acceptable salt forms or prodrugs thereof, wherein R^1, R^2, R^3, Y^1, Y^2, and A are defined below, are effective inhibitors of HCV NS3 protease.

BRIEF DESCRIPTION OF THE DRAWINGS

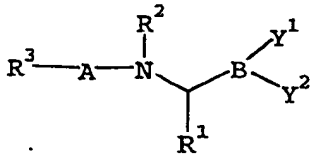
FIG. 1 illustrates plasmid construction maps for expression in cultured cells of HCV NS3 protease (pCMV NS3 PR) and substrate (pCMVNS5A/5B).

FIG. 2 illustrates detection by western blotting of NS3 protease-inhibitory compound in a cell-based assay. Human

293 cells were electroporated with expression plasmids described in FIG. 1. The cells were placed in tissue culture medium containing the indicated concentration of Example 10, an inhibitor of NS3 protease. The cells were allowed to synthesize proteins for 24 additional hours. Then the contents of the cells were analyzed using polyacrylamide gel electrophoresis and western blotting. The full length substrate (NS5A/5B) and cleavage product NS5A were detected with specific antiserum. Activity of the tested compound was measured by the accumulation of uncleaved NS5A/5B.

DETAILED DESCRIPTION OF THE INVENTION

Thus, in a first embodiment, the present invention provides a method of treating Hepatitis C virus in a mammal comprising administering to said mammal in need of such treatment an effective amount of a compound of Formula (I):



(I)

or a pharmaceutically acceptable salt form thereof, wherein:

Y^1 and Y^2 are independently selected from:

a) -OH,

b) -F,

c) $-NR^{18}R^{19}$,

d) C_1-C_8 alkoxy, or

when taken together, Y^1 and Y^2 form:

e) a cyclic boron ester where said chain or ring contains from 2 to 20 carbon atoms, and, optionally, 1, 2, or 3 heteroatoms which can be N, S, or O,

f) a cyclic boron amide where said chain or ring contains from 2 to 20 carbon atoms and, optionally, 1, 2, or 3 heteroatoms which can be N, S, or O,

g) a cyclic boron amide-ester where said chain or ring contains from 2 to 20 carbon atoms and, optionally, 1, 2, or 3 heteroatoms which can be N, S, or O;

R^1 is selected from:
$-CH=CH_2$, $-CH_2CH=CH_2$, $-CH=CHCH_3$,
$-C\equiv CH$, $-C\equiv CCH_3$, $-CH_2C\equiv CH$,
cyclopropyl, $-CH_2$cyclopropyl, cyclobutyl, $-CH_2$cyclobutyl,
$-(C_1-C_3$ alkyl$)SR^{1A}$, $-CH_2SR^{1A}$, $-CH(CH_3)SR^{1A}$, $-CH_2CH_2SR^{1A}$, $-CH_2CH_2CH_2SR^{1A}$, $-CH_2CH(CH_3)SR^{1A}$,
$-(C_1-C_3$ alkyl$)S-SR^{1B}$, $-CH_2S-SR^{1B}$, $-CH_2CH_2S-SR^{1B}$, $-CH(CH_3)S-SR^{1B}$,
$-(C_1-C_3$ alkyl$)S-CO_2R^{1A}$, $-CH_2S-CO_2R^{1A}$, $-CH_2CH_2S-CO_2R^{1A}$,
$-(C_1-C_3$ alkyl$)CO_2R^{1A}$, $-CH_2CO_2R^{1A}$, $-CH_2CH_2CO_2R^{1A}$,
C_1-C_4 haloalkyl, $-CF_3$, $-CF_2CF_3$, $-CF_2CF_2CF_3$, $-CF_2CF_2CF_2CF_3$, $-CF_2CHF_2$, $-CH_2CHF_2$, $-CH_2CH_2F$, $-CH_2CH_2CF_3$, $-CH_2CH_2CHF_2$, and $-CH_2CH_2CH_2F$;

R^{1A} is H, C_1-C_4 alkyl, phenyl, or $-CH_2$phenyl, wherein phenyl of R^{1A} is substituted with 0-3 substituents selected from $-CH_3$, $-CF_3$, $-NO_2$, $-CN$, $-OH$, $-SH$, $-OCH_3$, $-OCF_3$, $-Cl$, $-Br$, $-I$, and F;

R^{1B} is C_1-C_4 alkyl, phenyl, or $-CH_2$phenyl, wherein phenyl of R^{1B} is substituted with 0-3 substituents selected from $-CH_3$, $-CF_3$, $-NO_2$, $-CN$, $-OH$, $-SH$, $-OCH_3$, $-OCF_3$, $-Cl$, $-Br$, $-I$, and F;

A is a bond, A^1, A^1-A^2, $A^1-A^2-A^3$, $A^1-A^2-A^3-A^4$, $A^1-A^2-A^3-A^4-A^5$, $A^1-A^2-A^3-A^4-A^5-A^6$, $A^1-A^2-A^3-A^4-A^5-A^6-A^7$, $A^1-A^2-A^3-A^4-A^5-A^6-A^7-A^8$, $A^1-A^2-A^3-A^4-A^5-A^6-A^7-A^8-A^9$; or $A^1-A^2-A^3-A^4-A^5-A^6-A^7-A^8-A^9-A^{10}$;

A^1, A^2, A^3, A^4, A^5, A^6, A^7, A^8, A^9, and A^{10} are independently selected from an amino acid residue, wherein said amino acid residue comprises a natural amino acid, a modified amino acid or an unnatural amino acid;

R^2 is H, C_1-C_4 alkyl, aryl, aryl(C_1-C_4 alkyl)-, or C_3-C_6 cycloalkyl,

R^3 is H, $-C(=O)-X-(CH_2)_m-Z$, C_1-C_4 alkyl, C_2-C_4 alkenyl, C_2-C_4 alkynyl, C_1-C_3 alkyl-R^4, C_2-C_4 alkenyl-R^4, C_2-C_4 alkynyl-R^4, $-C(=O)R^4$, $-CO_2R^4$, $-S(=O)R^4$, $-S(=O)_2R^4$, $-C(=O)NHR^4$, aryl, aryl(C_1-C_4 alkyl)-, wherein aryl is optionally substituted with 0-3 substituents selected from $-CH_3$, $-NO_2$, -CN, -OH, $-OCH_3$, $-SO_2CH_3$, $-CF_3$, -Cl, -Br, -I, and -F; or an NH_2-blocking group;

R^4 is C_1-C_4 alkyl substituted with 0-1 R^{4A},
C_3-C_6 cycloalkyl substituted with 0-3 R^{4B} and
aryl substituted with 0-3 R^{4B} and
5-14 membered heterocyclic ring system consisting of carbon atoms and 1-4 heteroatoms selected from the group: O, S, and N, and said heterocyclic ring system is substituted with 0-3 R^{4B};

R^{4A} is C_1-C_4 alkyl, halo, $-OR^{20}$, $-SR^{20}$, $-NR^{18}R^{19}$,
phenyl substituted with 0-3 R^{4B};
naphthyl substituted with 0-3 R^{4B};
benzyl substituted with 0-3 R^{4B}; or a
5-6 membered heterocyclic ring system containing 1, 2 or 3 heteroatoms selected from nitrogen, oxygen and sulfur; said heterocyclic ring system is substituted with 0-3 R^{4B};

R^{4B} is selected at each occurrence from the group:

H, F, Cl, Br, I, $-NO_2$, -CN, -NCS, $-CF_3$, $-OCF_3$, $-CH_3$, $-CH_2CH_3$, $-OCH_3$, =O, OH, $-CO_2H$, $-SCH_3$, $-SO_3H$, $-SO_2CH_3$, $-NH_2$, $-NH(CH_3)$, $-N(CH_3)_2$, phenyl, $-CO_2R^{21}$, $-C(=O)NR^{21}R^{21}$, $-NHC(=O)R^{21}$, $-NR^{21}R^{21}$, $-OR^{21a}$, $-SR^{21a}$, $-C(=O)R^{21a}$, $-S(=O)R^{21a}$, $-SO_2R^{21}$, $-SO_2NR^{21}R^{21}$, C_1-C_4 haloalkyl, C_1-C_4 haloalkoxy, C_1-C_4 thioalkoxy, C_1-C_4 alkyl substituted with 0-3 R^{4C}, C_1-C_4 alkoxy substituted with 0-3 R^{4C}, C_3-C_6 cycloalkyl substituted with 0-3 R^{4C}, aryl substituted with 0-5 R^{4C}, and aryl(C_1-C_4 alkyl)- substituted with 0-5 R^{4C}, and 5-6 membered heterocyclic ring system consisting of carbon atoms and 1-3 heteroatoms selected from the group: O, S, and N, and said heterocyclic ring system is substituted with 0-4 R^{4C};

R^{4C} is selected at each occurrence from the group: H, F, Cl, Br, I, $-NO_2$, -CN, -NCS, $-CF_3$, $-OCF_3$, $-CH_3$, $-OCH_3$, =O, OH, $-CO_2H$, $-SO_2CH_3$, $-NH_2$, $-NH(CH_3)$, $-N(CH_3)_2$, phenyl, $-CO_2R^{21}$, $-C(=O)NR^{21}R^{21}$, $-NHC(=O)R^{21}$, $-NR^{21}R^{21}$, $-OR^{21a}$, $-SR^{21a}$, $-C(=O)R^{21a}$, $-S(=O)R^{21a}$, $-SO_2R^{21}$, $-SO_2NR^{21}R^{21}$, C_1-C_4 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, and C_1-C_4 haloalkoxy;

X is a bond, C_1-C_4 alkyl substituted with 0-3 R^{11}, C_2-C_4 alkenyl substituted with 0-2 R^{11}, C_3-C_{10} carbocycle substituted with 0-2 R^{11}, C_6-C_{10} aryl substituted with 0-3 R^{11}, or 5-10 membered heterocyclic ring system consisting of carbon atoms and 1-4 heteroatoms selected from the group: O, S, and N, and said heterocyclic ring system is substituted with 0-2 R^{11};

R^{11} at each occurrence is independently selected from

H, $-CH_3$, $-CH_2CH_3$, $-NO_2$, $-NH_2$, $-NH(CH_3)$, $-N(CH_3)_2$, $-SO_3H$, $-SO_2CH_3$, $-CO_2H$, $-CF_3$, $-OH$, $-OCH_3$, $-SCH_3$, $-OCF_3$, -Cl, -Br, -I, -F, =O, -CN, -NCS;

C_2-C_4 alkyl, C_2-C_4 alkoxy, C_2-C_4 thioalkoxy, C_1-C_4 haloalkyl, C_1-C_4 haloalkoxy, $-CO_2R^{21}$, $-C(=O)NR^{21}R^{21}$, $-NHC(=O)R^{21}$, $-NR^{21}R^{11}$, $-OR^{21a}$, $-SR^{21a}$, $-C(=O)R^{21a}$, $-S(=O)R^{21a}$, $-SO_2R^{21}$, $-SO_2NR^{21}R^{21}$, aryl, and aryl(C_1-C_4 alkyl)-, wherein aryl is optionally substituted with 0-3 substituents selected from $-CH_3$, $-NO_2$, -CN, -OH, $-OCH_3$, $-SO_2CH_3$, $-CF_3$, -Cl, -Br, -I, and F;

alternatively, two independent R^{11} groups may optionally be taken together to form $-(CH_2)_p-$;

m is 0, 1, 2, 3, or 4;

p is 1, 2, 3, or 4;

Z is selected from:

-H, $-R^{12}$, -halo, $-NHSO_2R^{12}$, $-SO_2NHR^{12}$, $-SO_2R^{12}$, $-C(=O)R^{12}$, $-OC(=O)C(=O)NHR^{12}$, $-NHC(=O)C(=O)OR^{12}$, $-OC(=O)R^{12}$, $-C(=O)OR^{12}$, $-OR^{12}$, $-SR^{12}$, and -CN;

R^{12} is H,

C_1-C_4 alkyl substituted with 0-3 R^{13},

C_3-C_{10} carbocycle substituted with 0-3 R^{13},

C_6-C_{10} aryl substituted with 0-3 R^{13}, or

5-10 membered heterocyclic ring system consisting of carbon atoms and 1-4 heteroatoms selected from the group: O, S, and N, and said heterocyclic ring system is substituted with 0-3 R^{13};

R^{13} at each occurrence is independently selected from H, $-CH_3$, $-CH_2CH_3$, $-NO_2$, $-SO_2OH$, $-SO_2CH_3$, CF_3, -Cl, -Br, -I, F, $-NH_2$, $-NH(CH_3)$, $-N(CH_3)_2$, $-NH(CH_2CH_3)$,

$-N(CH_2CH_3)_2$, and C_1-C_4 alkyl;

R^{18} and R^{19} at each occurrence are independently selected from H, C_1-C_4 alkyl, aryl(C_1-C_4 alkyl)-, and C_3-C_7 cycloalkyl;

R^{20} is C_1-C_4 alkyl;

R^{21} is, at each occurrence, independently H or C_1-C_4 alkyl; and

R^{21a} is, at each occurrence, independently H, C_1-C_4 alkyl, aryl, or C_1-C_4 haloalkyl;

provided when R^1 is $-CH_2CH=CH_2$, then A is not
-Asp-Glu-(2-methyl-Phe)-(3-methyl-Val)-Leu-,
-Asp-Glu-(2-methyl-Phe)-(3-methyl-Val)-(cyclopentyl-Ala)-,
-Asp-Glu-(2-methyl-Phe)-(cyclohexyl-Ala)-Leu-,
-Asp-Glu-(2-methyl-Phe)-(phenyl-Gly)-Leu-,
-Asp-Glu-(2-methyl-Phe)-(cyclohexyl-Ala)-Leu-,
-Asp-Glu-(2-methyl-Phe)-(3-methyl-Val)-(Pro)-,
-Asp-Glu-(2-methyl-Phe)-Phe-Leu-, or
-Asp-Glu-(4-chloro-2-methyl-Phe)-(3-methyl-Val)-(Leu)-.

[2] In a preferred embodiment of the present invention, provides for a method wherein A^1, A^2, A^3, A^4, A^5, A^6, A^7, A^8, A^9, and A^{10} are independently selected from an amino acid residue wherein said amino acid residue comprises a natural amino acid selected from the group: Ala, Arg, Ash, Asp, Aze, Cha, Cys, Dpa, Gln, Glu, Gly, His, Hyp, Ile, Irg, Leu, Lys, Met, Orn, Phe, Phe(4-fluoro), Pro, Sar, Ser, Thr, Trp, Tyr, and Val; a modified amino acid selected from the group: Asp(OMe), Glu(OMe), Hyp(OMe), Asp(O^tBu), Glu(O^tBu), Hyp(O^tBu), Thr(O^tBu), Asp(OBzl), Glu(OBzl), Hyp(OBzl), Thr(OBzl); and an unnatural amino acid selected from the group:
2-aminobutanoic acid, 2-aminopentanoic acid,

2-aminohexanoic acid, 2-aminoheptanoic acid,
2-aminooctanoic acid, 2-aminononanoic acid,
2-aminodecanoic acid, 2-aminoundecanoic acid,
2-amino-3,3-dimethylbutanoic acid,
2-amino-4,4-dimethylpentanoic acid,
2-amino-3-methylhexanoic acid,
2-amino-3-methylheptanoic acid,
2-amino-3-methyloctanoic acid,
2-amino-3-methylnonanoic acid,
2-amino-4-methylhexanoic acid,
2-amino-3-ethylpentanoic acid,
2-amino-3,4-dimethylpentanoic acid,
2-amino-3,5-dimethylhexanoic acid,
2-amino-3,3-dimethylpentanoic acid,
2-amino-3-ethyl-3-methylpentanoic acid,
2-amino-3,3-diethylpentanoic acid,
2-amino-5-methylhexanoic acid, 2-amino-6-methylheptanoic,
2-amino-7-methyloctanoic, 2-amino-2-cyclopentylacetic,
2-amino-2-cylcohexylacetic acid,
2-amino-2-(1-methylcylcohexyl)acetic acid,
2-amino-2-(2-methyl-1-methylcylcohexyl)acetic acid,
2-amino-2-(3-methyl-1-methylcylcohexyl)acetic acid,
2-amino-2-(4-methyl-1-methylcylcohexyl)acetic acid,
2-amino-2-(1-ethylcycolhexyl)acetic acid,
2-amino-3-(cyclohexyl)propanoic acid,
2-amino-4-(cyclohexyl)butanoic acid,
2-amino-3-(1-adamantyl)propanoic acid,
2-amino-3-butenoic acid, 2-amino-3-methyl-3-butenoic acid,
2-amino-4-pentenoic acid, 2-amino-4-hexenoic acid,
2-amino-5-heptenoic acid, 2-amino-4-methyl-4-hexenoic acid,
2-amino-5-methyl-4-hexenoic acid,
2-amino-4-methy-5-hexenoic acid, 2-amino-6-heptenoic acid,
2-amino-3,3,4-trimethyl-4-pentenoic acid,
2-amino-4-chloro-4-pentenoic,
2-amino-4,4-dichloro-3-butenoic acid,
2-amino-3-(2-methylenecyclopropyl)-propanoic acid,
2-amino-2-(2-cyclopentenyl)acetic acid,
2-amino-2-(cyclohexenyl)acetic acid,

2-amino-3-(2-cyclopentenyl)propanoic acid,
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2-amino-3-(1-cycloheptenyl)propanoic acid,
2-amino-3-(1,4-cyclohexadienyl)propanoic acid,
2-amino-3-(2,5-cyclohexadienyl)propanoic acid,
2-amino-2-(7-cycloheptatrienyl)acetic acid,
2-amino-4,5-hexadienoic acid,
2-amino-3-butynoic acid, 2-amino-4-pentyoic acid,
2-amino-4-hexynoic acid, 2-amino-4-hepten-6-ynoic acid,
2-amino-3-fluoropropanoic acid,
2-amino-3,3,3-trifluoropropanoic acid,
2-amino-3-fluorobutanoic acid,
2-amino-3-fluoropentanoic acid,
2-amino-3-fluorohexanoic acid,
2-amino-3,3-difluorobutanoic acid,
2-amino-3,3-difluoro-3-phenylpropanoic acid,
2-amino-3-perfluoroethylpropanoic acid,
2-amino-3-perfluoropropylpropanoic acid,
2-amino-3-fluoro-3-methylbutanoic acid,
2-amino-5,5,5-trifluoropentanoic acid,
2-amino-3-methyl-4,4,4-trifluorobutanoic acid,
2-amino-3-trifluoromethyl-4,4,4-trifluorobutanoic acid,
2-amino-3,3,4,4,5,5-heptafluoropentanoic acid,
2-amino-3-methyl-5-fluoropentanoic acid,
2-amino-3-methyl-4-fluoropentanoic acid,
2-amino-5,5-difluorohexanoic acid,
2-amino-4-(fluoromethyl)-5-fluoropentanoic acid,
2-amino-4-trifluoromethyl-5,5,5-trifluoropentanoic acid,
2-amino-3-fluoro-3-methylbutanoic acid,
2-amino-3-fluoro-3-phenylpentanoic acid,
2-amino-2-(1-fluorocyclopentyl)acetic acid,
2-amino-2-(1-fluorocyclohexyl)acetic acid,
2-amino-3-chloropropanoic acid acid,

2-amino-3-chlorobutanoic acid acid,
2-amino-4,4-dichlorobutanoic acid acid,
2-amino4,4,4-trichlorobutanoic acid,
2-amino-3,4,4-trichlorobutanoic acid,
2-amino-6-chlorohexanoic acid,
2-amino-4-bromobutanoic acid,
2-amino-3-bromobutanoic acid,
2-amino-3-mercaptobutanoic acid,
2-amino-4-mercaptobutanoic acid,
2-amino-3-mercapto-3,3-dimethylpropanoic acid,
2-amino-3-mercapto-3-methylpentanoic acid,
2-amino-3-mercaptopentanoic acid,
2-amino-3-mercapto-4-methylpentanoic acid,
2-amino-3-methyl-4-mercaptopentanoic acid,
2-amino-5-mercapto-5-methylhexanoic acid,
2-amino-2-(1-mercaptocyclobutyl)acetic acid,
2-amino-2-(1-mercaptocyclopentyl)acetic acid,
2-amino-2-(1-mercaptocyclohexyl)acetic acid,
2-amino-5-(methylthio)pentanoic acid,
2-amino-6-(methylthio)hexanoic acid,
2-amino-4-methylthio-3-phenylbutanoic acid,
2-amino-5-ethylthio-5-methylpentanoic acid,
2-amino-5-ethylthio-3,5,5-trimethylpentanoic acid,
2-amino-5-ethylthio-5-phenylpentanoic acid,
2-amino-5-ethylthio-5-pentanoic acid,
2-amino-5-butylthio-5-methylpentanoic acid,
2-amino-5-butylthio-3,5,5-trimethylpentanoic acid,
2-amino-5-butylthio-5-phenylpentanoic acid,
2-amino-5-(butylthio)pentanoic acid,
2-amino-3-methy4-hydroselenopentanoic acid,
2-amino-4-methylselenobutanoic acid,
2-amino-4-ethylselenobutanoic acid,
2-amino-4-benzylselenobutanoic acid,
2-amino-3-methyl-4-(methylseleno)butanoic acid,
2-amino-3-(aminomethylseleno)propanoic acid,
2-amino-3-(3-aminopropylseleno)propanoic acid,
2-amino-4-methyltellurobutanoic acid,
2-amino-4-hydroxybutanoic acid,

2-amino-4-hydroxyhexanoic acid,
2-amino-3-hydroxypentanoic acid,
2-amino-3-hydroxyhexanoic acid,
2-amino-3methyl-4-hydroxybutanoic acid,
2-amino-3-hydroxy-3-methylbutanoic acid,
2-amino-6-hydroxyhexanoic acid,
2-amino-4-hydroxyhexanoic acid,
2-amino-3-hydroxy-4-methylpentanoic acid,
2-amino-3-hydroxy-3-methylpentanoic acid,
2-amino4-hydroxy-3,3-dimethylbutanoic acid,
2-amino-3-hydroxy4-methylpentanoic acid,
2-amino-3-hydroybutanedioic acid,
2-amino-3-hydroxy-3-phenyl-propanoic acid,
2-amino-3-hydroxy-3-(4-nitrophenyl)propanoic acid,
2-amino-3-hydroxy-3-(3-pyridyl)propanoic acid,
2-amino-2-(1-hydroxycyclopropyl)acetic acid,
2-amino-3-(1-hydroxycyclohexyl)propanoic acid,
2-amino-3-hydroxy-3-phenylpropanoic acid,
2-amino-3-hydroxy-3-[3-bis(2-
chloroethyl)aminophenyl]propanoic acid,
2-amino-3-hydroxy-3-(3,4-dihydroxyphenyl)propanoic acid,
2-amino-3-hydroxy-3-(3,4-methylenedioxyphenyl)propanoic
acid,
2-amino-4-fluoro-3-hydroxybutanoic acid,
2-amino-4,4,4-trichloro-3-hydroxybutanoic acid,
2-amino-3-hydroxy-4-hexynoic acid,
2-amino-3,4-dihydroxybutanoic acid,
2-amino-3,4,5,6-tetrahydroxyhexanoic acid,
2-amino-4,5-dihydroxy-3-methylpentanoic acid,
2-amino-5,6-dihydroxyhexanoic acid,
2-amino-5-hydroxy-4-(hydroxyrnethyl)pentanoic acid,
2-amino-4,5-dihydroxy-4-(hydroxymethyl)pentanoic acid,
2-amino-3-hydroxy-5-benzyloxypentanoic acid,
2-amino-3-(2-aminoethoxy)propanoic acid,
2-amino-4-(2-aminoethoxy)butanoic acid,
2-amino-4-oxobutanoic acid,
2-amino-3-oxobutanoic acid,
2-amino-4-methyl-3-oxopentanoic acid,

2-amino-3-phenyl-3-oxopropanoic acid,
2-amino-4-phenyl-3-oxobutanoic acid,
2-amino-3-methyl-4-oxopentanoic acid,
2-amino-4-oxo-4-(4-hydroxyphenyl)butanoic acid,
2-amino-4-oxo-4-(2-furyl)butanoic acid,
2-amino-4-oxo-4-(2-nitrophenyl)butanoic acid,
2-amino-4-oxo-4-(2-amino-4-chlorophenyl)butanoic acid,
2-amino-3-(4-oxo-1-cyclohexenyl)propanoic acid,
2-amino-3-(4-oxocyclohexanyl)propanoic acid,
2-amino-3-(2,5-dimethyl-3,6-dioxo-1,4-cydohexadienyl)propanoic acid,
2-amino-3-(1-hydroxy-5-methyl-7-oxo-cyclohepta-1,3,5-trien-2-yl)propanoic acid,
2-amino-3-(1-hydroxy-7-oxo-cyclohepta-1,3,5-trien-3-yl)propanoic acid,
2-amino-3-(1-hydroxy-7-oxo-cyclohepta-1,3,5-trien-4-yl)propanoic acid,
2-amino-4-methoxy-3-butenoic acid,
2-amino-4-(2-aminoethoxy)-3-butenoic acid,
2-amino-4-(2-amino-3-hydroxypropyl)-3-butenoic acid,
2-amino-2-(4-methoxy-1,4-cyclohexadienyl)acetic acid,
2-amino-3,3-diethoxypropanoic acid,
2-amino-4,4-dimethylbutanoic acid,
2-amino-2-(2,3-epoxycyclohexyl)acetic acid,
2-amino-3-(2,3-epoxycyclohexy)propanoic acid,
2-amino-8-oxo-9,10-epoxydecanoic acid,
2-amino-propanedioic acid,
2-amino-3-methylbutanedioic acid,
2-amino-3,3-dimethylbutanedioic acid,
2-amino4-methylpentanedioic acid,
2-amino-3-methylpentanedioic acid,
2-amino-3-phenylpentanedioic acid,
2-amino-3-hydroxypentanedioic acid,
2-amino-3-carboxypentanedioic acid,
2-amino-4-ethylpentanedioic acid,
2-amino-4-propylpentanedioic acid,
2-amino-4-isoamylpentanedioic acid,
2-amino-4-phenylpentanedioic acid,

2-amino-hexanedioic acid, 2-amino-heptanedioic acid,
2-amino-decanedioic acid, 2-amino-octanedioic acid,
2-amino-dodecanedioic acid,
2-amino-3-methylenebutanedioic acid,
2-amino-4-methylenepentanedioic acid,
2-amino-3-fluorobutanedioic acid,
2-amino-4-fluoropentanedioic acid,
2-amino-3,3-difluorobutanedioic acid,
2-amino-3-chloropentanedioic acid,
2-amino-3-hydroxybutanedioic acid,
2-amino-4-hydroxypentanedioic acid,
2-amino-4-hydroxyhexanedioic acid,
2-amino-3,4-dihydroxypentanedioic acid,
2-amino-3-(3-hydroxypropyl)butanedioic acid,
2-amino-3-(1-carboxy-4-hydroxy-2-cyclodienyl)propanoic acid,
2-amino-3-(aceto)butanedioic acid,
2-amino-3-cyanobutanedioic acid,
2-amino-3-(2-carboxy-6-oxo-6H-pyranyl)propanoic acid,
2-amino-3-carboxybutanedioic acid,
2-amino-4-carboxypentanedioic acid,
3-amido-2-amino-3-hydroxypropanoic acid,
3-arnido-2-amino-3-methylpropanoic acid,
3-amido-2-amino-3-phenylpropanoic acid,
3-amido-2,3-diaminopropanoic acid,
3-amido-2-amino-3-[N-(4-hydroxyphenyl)amino]propanoic acid,
2,3-diaminopropanoic acid, 2,3-diaminobutanoic acid,
2,4-diaminobutanoic acid,
2,4-diamino-3-methylbutanoic acid,
2,4-diamino-3-phenylbutanoic acid,
2-amino-3-(methylamino)butanoic acid,
2,5-diamino-3-methylpentanoic acid,
2,7-diaminoheptanoic acid,
2,4-diaminoheptanoic acid, 2-amino-2-(2-piperidyl)acetic acid,
2-amino-2-(1-aminocyclohexyl)acetic acid,
2,3-diamino-3-phenylpropanoic acid,
2,3-diamino-3-(4-hydroxyphenyl)propanoic acid,

2,3-diamino-3-(4-methoxyphenyl)propanoic acid,
2,3-diamino-3-[4-(N,N'-dimethyamino)phenyl]propanoic acid,
2,3-diamino-3-(3,4-dimethoxyphenyl)propanoic acid,
2,3-diamino-3-(3,4-methylenedioxyphenyl)propanoic acid,
2,3-diamino-3-(4-hydroxy-3-methoxyphenyl)propanoic acid,
2,3-diamino-3-(2-phenylethyl)propanoic acid,
2,3-diamino-3-propylpropanoic acid,
2,6-diamino-4-hexenoic acid,
2,5-diamino-4-fluoropentanoic acid,
2,6-diamino-5-fluorohexanoic acid,
2,6-diamino-4-hexynoic acid,
2,6-diamino-5,5-difluorohexanoic acid,
2,6-diamino-5,5-dimethylhexanoic acid,
2,5-diamino-3-hydroxypentanoic acid,
2,6-diamino-3-hydroxyhexanoic acid,
2,5-diamino-4-hydroxypentanoic acid,
2,6-diamino-4-hydroxyhexanoic acid,
2,6-diamino-4-oxohexanoic acid,
2,7-diaminooctanedioic acid,
2,6-diamino-3-carboxyhexanoic acid,
2,5-diamino-4-carboxypentanoic acid,
2-amino-4-(2-(N,N'-diethylamino)ethyl)pentandioic acid,
2-amino-4-(N,N'-diethylamino)pentandioic acid,
2-amino-4-(N-morpholino)pentandioic acid,
2-amino-4-(N,N'-bis(2-chloroethyl)amino)pentandioic acid,
2-amino-4-(N,N'-bis(2-hydroxyethyl)amino)pentandioic acid,
2,3,5-triaminopentanoic acid,
2-amino-3-(N-(2-aminethyl)amino)propanoic acid,
2-amino-3-((2-aminoethyl)seleno)propanoic acid,
2-amino-3-[(2-aminoethyl)thio]propanoic acid,
2-amino4-aminooxybutanoic acid,
2-amino-5-hydroxyaminopentanoic acid,
2-amino-5-[N-(5-nitro-2-pyrimidinyl)amino]pentanoic acid,
2-amino-4-[(7-nitro-2,1,3-benzoxadiazol-4-yl)amino]butanoic acid,
2-amino-3-guanidinopropanoic acid,
2-amino-3-guanidinobutanoic acid,
2-amino-4-guanidobutanoic acid,

2-amino-6-guanidohexanoic acid,
2-amino-6-ureidohexanoic acid,
2-amino-3-(2-iminoimidiazolin-4-yl)propanoic acid,
2-amino-2-(2-iminohexahydropyrimidin-4-yl)acetic acid,
2-amino-3-(2-iminohexahydropyrimidiny-4-yl)propanoic acid,
2-amino4-fluoro-5-guanidopentanoic acid,
2-amino-4-hydroxy-5-guanidopentanoic acid,
2-amino-4-guanidooxybutanoic acid,
2-amino-6-amidinohexanoic acid,
2-amino-5-(N-acetimidoylamino)pentanoic acid,
1-aminocyclopropanecarboxylic acid,
1-amino4-ethylcyclpropanecarboxylic acid,
1-aminocyclopentanecarboxylic acid,
1-aminocyclopentanecarboxylic acid,
1-amino-2,2,5,5-tetramethyl-cyclohexanecarboxylic acid,
1-aminocydoheptanecarboxylic acid,
1-aminocyclononanecarboxylic acid,
2-aminoindan-2-carboxylic acid,
2-aminonorbornane-2-carboxylic acid,
2-amino-3-phenylnorbornane-2-carboxylic acid,
3-aminotetrahydrothiophene-3-carboxylic acid,
1-amino-1,3-cyclohexanedicarboxylic acid,
3-aminopyrrolidine-3-carboxylic acid,
1,4-diaminocyclohexanecarboxylic acid,
6-alkoxy-3-amino-1,2,3,4-tetrahydrocarbazole-3-carboxylic acid,
2- aminobenzobicyclo[2,2,2]octane-2-carboxylic acid,
2-aminoindan-2-carboxylic acid,
1-amino-2-(3,4-dhydroxyphenyl)cyclopropanecarboxylic acid,
5,6-dialkoxy-2-aminoindane-2-carboxylic acid,
4,5-dihydroxy-2-aminoindan-2-caroxylic acid,
5,6-dihydroxy-2-aminotetralin-2-carboxylic acid,
2-amino-2-cyanoacetic acid,
2-amino-3-cyanopropanoic acid,
2-amino-4-cyanobutanoic acid,
2-amino-5-nitropentanoic acid,
2-amino-6-nitrohexanoic acid,
2-amino-4-aminooxybutanoic acid,

2-amino-3-(N-nitrosohydroxyamino)propanoic acid,
2-amino-3-ureidopropanoic acid,
2-amino-4-ureidobutanoic acid,
2-amino-3-phosphopropanoic acid,
2-amino-3-thiophosphopropanoic acid,
2-amino-4-methanephosphonylbutanoic acid,
2-amino-3-(trimethylsilyl)propanoic acid,
2-amino-3-(dimethyl(trimethylsilylmethylsilyl)propanoic acid,
2-amino-2-phenylacetic acid,
2-amino-2-(3-chlorophenyl)acetic acid,
2-amino-2-(4-chlorophenyl)acetic acid,
2-amino-2-(3-fluorophenyl)acetic acid,
2-amino-2-(3-methylphenyl)acetic acid,
2-amino-2-(4ofluorophenyl)acetic acid,
2-amino-2-(4-methylphenyl)acetic acid,
2-amino-2-(4-methoxyphenyl)acetic acid,
2-amino-2-(2-fluorophenyl)acetic acid,
2-amino-2-(2-methylphenyl)acetic acid,
2-amino-2-(4-chloromethylphenyl)acetic acid,
2-amino-2-(4-hydroxymethylphenyl)acetic acid,
2-amino-2-[4-(methylthiomethyl)phenyl]acetic acid,
2-amino-2-(4-bromomethylphenyl)acetic acid,
2-amino-2-(4-(methoxymethy)phenyl)acetic acid,
2-amino-2-(4-((N-benzylamino)methyl)phenyl)acetic acid,
2-amino-2-(4-hydroxylphenyl)acetic acid,
2-amino-2-(3-hydroxylphenyl)acetic acid,
2-amino-2-(3-carboxyphenyl)acetic acid,
2-amino-2-(4-aminophenyl)acetic acid,
2-amino-2-(4-azidophenyl)acetic acid,
2-amino-2-(3-t-butyl-4-hydroxyphenyl)acetic acid,
2-amino-2-(3,5-difluoro-4-hydroxyphenyl)acetic acid,
2-amino-2-(3,5-dihydroxyphenyl)acetic acid,
2-amino-2-(3-carboxy-4-hydroxyphenyl)acetic acid,
2-amino-2-(3,5-di-t-butyl-4-hydroxyphenyl)acetic acid,
2-amino-3-(2-methylphenyl)propanoic acid,
2-amino-3-(4-ethylphenyl)propanoic acid,
2-amino-3-(4-phenylphenyl)propanoic acid,

2-amino-3-(4-benzylphenyl)propanoic acid,
2-amino-3-(3-fluorophenyl)propanoic acid,
2-amino-3-(4-methylphenyl)propanoic acid,
2-amino-3-(4-fluorophenyl)propanoic acid,
2-amino-3-(4-chlorophenyl)propanoic acid,
2-amino-3-(2-chlorophenyl)propanoic acid,
2-amino-3-(4-bromophenyl)propanoic acid,
2-amino-3-(2-bromophenyl)propanoic acid,
2-amino-3-(3-hydroxyphenyl)propanoic acid,
2-amino-3-(2-hydroxyphenyl)propanoic acid,
2-amino-3-(4-mercaptophenyl)propanoic acid,
2-amino-3-(3-trifluoromethylphenyl)propanoic acid,
2-amino-3-(3-hydroxyphenyl)propanoic acid,
2-amino-3-(4-hydroxyphenyl)propanoic acid,
2-amino-3-[4-(hydroxymethy)phenyl]propanoic acid,
2-amino-3-[3-(hydroxymethyl)phenyl]propanoic acid,
2-amino-3-[3-(aminomethyl)phenyl]propanoic acid,
2-amino-3-(3-carboxyphenyl)propanoic acid,
2-amino-3-(4-nitrophenyl)propanoic acid,
2-amino-3-(4-aminophenyl)propanoic acid,
2-amino-3-(4-azidophenyl)propanoic acid,
2-amino-3-(4-cyanophenyl)propanoic acid,
2-amino-3-(4-acetophenyl)propanoic acid,
2-amino-3-(4- guanidinophenyl)propanoic acid,
2-amino-3-[4-(phenylazo)phenyl]propanoic acid,
2-amino-3-[4-(2-phenylethylenyl)phenyl]propanoic acid,
2-amino-3-(4-trialkylsilylphenyl)propanoic acid,
2-amino-3-(2,4-dimethylphenyl)propanoic acid,
2-amino-3-(2,3-dimethylphenyl)propanoic acid,
2-amino-3-(2,5-dimethylphenyl)propanoic acid,
2-amino-3-(3,5-dimethylphenyl)propanoic acid,
2-amino-3-(2,4,6-trimethylphenyl)propanoic acid,
2-amino-3-(3,4,5-trimethylphenyl)propanoic acid,
2-amino-3-(2,3,4,5,6-pentamethylphenyl)propanoic acid,
2-amino-3-(2,4,-difluorophenyl)propanoic acid,
2-amino-3-(3,4,-difluorophenyl)propanoic acid,
2-amino-3-(2,5,-difluorophenyl)propanoic acid,
2-amino-3-(2,6,-difluorophenyl)propanoic acid,

2-amino-3-(2,3,5,6-tetrafluorophenyl)propanoic acid,
2-amino-3-(3,5-dichloro-2,4,6-trifluorophenyl)propanoic acid,
2-amino-3-(2,3-difluorophenyl)propanoic acid,
2-amino-3-(2,3-bistrifluoromethylphenyl)propanoic acid,
2-amino-3-(2,4-bistrifluoromethylphenyl)propanoic acid,
2-amino-3-(2-chloro-5-trifluoromethylphenyl)propanoic acid,
2-amino-3-(2,5-difluorophenyl)propanoic acid,
2-amino-3-(2,3,4,5,6-pentafluorophenyl)propanoic acid,
2-amino-3-(2,3-dibromophenyl)propanoic acid,
2-amino-3-(2,5-dibromophenyl)propanoic acid,
2-amino-3-(3,4-dibromophenyl)propanoic acid,
2-amino-3-(3,4,5-triiodophenyl)propanoic acid,
2-amino-3-(2,3-dihydroxyphenyl)propanoic acid,
2-amino-3-(2,5-dihydroxyphenyl)propanoic acid,
2-amino-3-(2,6-dihydroxyphenyl)propanoic acid,
2-amino-3-(3-bromo-5-methoxyphenyl)propanoic acid,
2-amino-3-(2,5-dimethoxyphenyl)propanoic acid,
2-amino-3-(2,5-dimethoxy-4-methylphenyl)propanoic acid,
2-amino-3-(4-bromo-2,5-dimethoxyphenyl)propanoic acid,
2-amino-3-(3-carboxy-4-hydroxyphenyl)propanoic acid,
2-amino-3-(3-carboxy-4-aminophenyl)propanoic acid,
2-amino-3-(2-hydroxy-5-nitrophenyl)propanoic acid,
2-amino-3-(2-ethoxy-5-nitrophenyl)propanoic acid,
2-amino-3-(3,4,5- trimethoxyphenyl)propanoic acid,
2-amino-3-(4-azido-2-nitrophenyl)propanoic acid,
2-amino-3-(2-hydroxy-5-nitrophenyl)propanoic acid,
2-amino-3-(2,4-bis-trimethylsilylphenyl)propanoic acid,
2-amino-3-(4-hydroxy-3,5-di-t-butylphenyl)propanoic acid,
2-amino-3-(4-hydroxy-3-benzylphenyl)propanoic acid,
2-amino-3-(4-hydroxy-3-fluorophenyl)propanoic acid,
2-amino-3-(4-hydroxy-2,3,5,6-tetrafluorophenyl)propanoic acid,
2-amino-3-(4-hydroxy-3,5-dichlorophenyl)propanoic acid,
2-amino-3-(4-hydroxy-3-iodophenyl)propanoic acid,
2-amino-3-(4-hydroxy-3,5-diiodophenyl)propanoic acid,
2-amino-3-(4-hydroxy-2-hydroxyphenyl)propanoic acid,
2-amino-3-(4-hydroxy-3-hydroxymethylphenyl)propanoic acid,

2-amino-3-(4-hydroxy-2-hydroxy-6-methylphenyl)propanoic acid,
2-amino-3-(4-hydroxy-3-carboxyphenyl)propanoic acid,
2-amino-3-(4-hydroxy-3,5-dinitrophenyl)propanoic acid,
substituted thyronines,
2-amino-3-(3,4-dihydroxy-2-chlorophenyl)propanoic acid,
2-amino-3-(3,4-dihydroxy-2-bromophenyl)propanoic acid,
2-amino-3-(3,4-dihydroxy-2-fluorophenyl)propanoic acid,
2-amino-3-(3,4-dihydroxy-2-nitrophenyl)propanoic acid,
2-amino-3-(3,4-dihydroxy-2-methylphenyl)propanoic acid,
2-amino-3-(3,4-dihydroxy-2-ethylphenyl)propanoic acid,
2-amino-3-(3,4-dihydroxy-2-isopropylphenyl)propanoic acid,
2-amino-3-(2-t-butyl-4,5-dihydroxyphenyl)propanoic acid,
2-amino-3-(3-fluoro-4,5-dihydroxyphenyl)propanoic acid,
2-amino-3-(2-fluoro-4,5-dihydroxyphenyl)propanoic acid,
2-amino-3-(2,5,6-trifluoro-3,4-dihydroxyphenyl)propanolc acid,
2-amino-3-(2,6-dibromo-3,4-dihydroxyphenyl)propanoic acid,
2-amino-3-(5,6-dibromo-3,4-dihydroxyphenyl)propanoic acid,
2-amino-3-(2,4,5-trihydroxyphenyl)propanoic acid,
2-amino-3-(2,3,4-trihydroxyphenyl)propanoic acid,
2-amino-3-(3,4-dihydroxy-5-methoxyphenyl)propanoic acid,
2-amino-3-methyl-3-phenylpropanoic acid,
2-amino-3-ethyl-3-phenylpropanoic acid,
2-amino-3-isopropyl-3-phenylpropanoic acid,
2-amino-3-butyl-3-phenylpropanoic acid,
2-amino-3-benzyl-3-phenylpropanoic acid,
2-amino-3-phenylethyl-3-phenylpropanoic acid,
2-amino-3-(4-chlorophenyl)-3-phenylpropanoic acid,
2-amino-3-(4-methoxyphenyl)-3-phenylpropanoic acid,
2-amino-3,3-diphenylpropanoic acid,
2-amino-3-[4-(N,N- diethylamino)phenyl]heptanoic acid,
2-amino-3-[4-(N,N-diethylamino)phenyl]pentanoic acid,
2-amino-3-(3,4-dimethoxyphenyl)pentanoic acid,
2-amino-3-(3,4-dihydroxyphenyl)pentanoic acid,
2-amino-3-methyl-3-phenylbutanoic acid,
2-amino-3-ethyl-3-phenylpentanoic acid,
2-amino-3-methyl-3-phenylpentanoic acid,

2-amino-3,3-diphenylbutanoic acid,
2-amino-3-fluoro-3-phenylpropanoic acid,
2-amino-3-methylene-3-phenylpropanoic acid,
2-amino-3-methylmercapto-3-phenylpropanoic acid,
2-amino-4-methylmercapto-4-phenylbutanoic acid,
2-amino-4-(3,4-dihydroxyphenyl)butanoic acid,
2-amino-5-(4-methoxyphenyl)pentanoic acid,
2-amino-4-phenylbutanoic acid,
2-amino-5-phenylpentanoic acid,
2-amino-3,3-dimethyl-5-phenylpentanoic acid,
2-amino-4-phenyl-3-butenoic acid,
2-amino-4-phenoxybutanoic acid,
2-amino-5-phenoxypentanoic acid,
2-amino-2-(indanyl)acetic acid,
2-amino-2-(1-tetralyl)acetic acid,
2-amino-4,4-diphenylbutanoic acid,
2-amino-2-(2-naphthyl)acetic acid,
2-amino-3-(1-naphthyl)propanoic acid,
2-amino-3-(1-naphthyl)pentanoic acid,
2-amino-3-(2-naphthyl)propanoic acid,
2-amino-3-(1-chloro-2-naphthyl)propanoic acid,
2-amino-3-(1-bromo-2-naphthyDpropanoic acid,
2-amino-3-(4-hydroxy-1-naphthyl)propanoic acid,
2-amino-3-(4-methoxy-1-naphthyl)propanoic acid,
2-amino-3-(4-hydroxy-2-chloro-1-naphthyl)propanoic acid,
2-amino-3-(2-chloro-4-methoxy-1-naphthyl)propanoic acid,
2-amino-2-(2-anthryl)acetic acid,
2-amino-3-(9-anthryl)propanoic acid,
2-amino-3-(2-fluorenyl)propanoic acid,
2-amino-3-(4-fluorenyl)propanoic acid,
2-amino-3-(carboranyl)propanoic acid,
3-methylproline, 4-methylproline, 5-methylproline,
4,4-dimethylproline, 4-fluoroproline,
4,4-difluoroproline, 4-bromoproline, 4-chloroproline,
3,4-dehydroproline, 4-methylproline,
4-methyleneproline, 4-mercaptoproline,
4-(4-methoxybenzylmercapto)proline, 4-hydroxymethylproline,
3-hydroxyproline, 3-hydroxy-5-methylproline,

3,4-dihydroxyproline, 3-phenoxyproline,
3-carbamylalkylproline, 4-cyano-5-methyl-5-carboxyproline,
4,5-dicarboxyl-5-methylproline, 2-aziridinecarboxylic acid,
2-azetidinecarboxylic acid,
4-methyl-2-azetidinecarboxylic acid, pipecolic acid,
1,2,3,6-tetrahydropicolinic acid, 3,4-methyleneproline,
2.4-methyleneproline, 4-aminopipecolic acid,
5-hydroxypipecolic acid, 4,5-dihydroxypipecolic acid,
5,6-dihydroxy-2,3-dihydroindole-2-carboxylic acid,
1,2,3,4-tetrahydroquinoline-2-carboxylic acid,
6,7-dihydroxy-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid,
6-hydroxy-1-methyl-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid,
6,7-dihydroxy-1-methyl-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid,
1,3-oxazolidine-4-carboxylic acid,
1,2-oxazolidine-3-carboxylic acid,
perhydro-1,4-thiazine-3-carboxylic acid,
2,2-dimethylthiazolidine-4-carboxylic acid,
perhydro-1,3-thlazine-2-carboxylic acid,
selenazolidine4-carboxylic acid,
2-phenylthiazolidine4-carboxylic acid,
2-(4-carboxylicyl)thiazolidine-4-carboxylic acid,
1,2,3,4,4a,9a-hexahydro-beta-carboline-3-carboxylic acid,
2,3,3a,8a-tetrahydropyrrolo(2,3b)indole-2-carboxylic acid,
2-amino-3-(2-pyridyl)propanoic acid,
2-amino-3-(3-pyridyl)propanoic acid,
2-amino-3-(4-pyridyl)propanoic acid,
2-amino-3-(2-bromo-3-pyridyl)propanoic acid,
2-amino-3-(2-bromo-4-pyridyl)propanoic acid,
2-amino-3-(2-bromo-5-pyridyl)propanoic acid,
2-amino-3-(2-bromo-6-pyridyl)propanoic acid,
2-amino-3-(2-chloro-3-pyridyl)propanoic acid,
2-amino-3-(2-chloro-4-pyridyl)propanoic acid,
2-amino-3-(2-chloro-5-pyridyl)propanoic acid,
2-amino-3-(2-chloro-6-pyridyl)propanoic acid,
2-amino-3-(2-fluoro-3-pyridyl)propanoic acid,

2-amino-3-(2-fluoro-4-pyridyl)loropanoic acid,
2-amino-3-(2-fluoro-5-pyridyl)propanoic acid,
2-amino-3-(2-fluoro-6-pyridyl)proloanoic acid,
2-amino-3-(1,2-dihydro-2-oxo-3-pyridyl)propanoic acid,
2-amino-3-(1,2-dihydro-2-oxo4-pyridyl)propanoic acid,
2-amino-3-(1,2-dihydro-2-oxo-5-pyridyl)propanoic acid,
2-amino-3-(1,2-dihydro-2-oxo-6-pyridyl)propanoic acid,
2-amino-3-(5-hydroxy-2-pyridyl)propanoic acid,
2-amino-3-(5-hydroxy-6-iodo-2-pyridyl)propanoic acid,
2-amino-3-(3-hydroxy-4-oxo-1,4dihydro-1-pyridyl)propanoic acid,
N-(5-caroxyl-5-aminopentyl)pyridinium chloride,
1,2,5-trimethyl-4-(2-amino-2-carboxy-1-hydroxyethyl)pyridinium chloride,
2-amino-2-(5-chloro-2-pyridyl)acetic acid,
N-(3-amino-3-carboxypropyl)pyridinium chloride,
2-amino-3-(2-pyrryl)propanoic acid,
2-amino-3-(1-pyrryl)propanoic acid,
2-amino-4-(1-pyrryl)butanoic acid,
2-amino-5-(1-pyrryl)pentanoic acid,
2-amino-3-(5-imidazolyl)-3-methylpropanoic acid,
2-amino-3-(5-imidazolyl)-3-ethylpropanoic acid,
2-amino-3-hexyl-3-(5-imidazolyl)propanoic acid,
2-amino-3-hydroxy-3-(5-imidazolyl)propanoic acid,
2-amino-3-(4-nitro-5-imidazolyl)proloanoic acid,
2-amino-3-(4-methyl-5-imidazolyl)propanoic acid,
2-amino-3-(2-methyl-5-imidazolyl)propanoic acid,
2-amino-3-(4-fluoro-5-imidazolyl)propanoic acid,
2-amino-3-(2-fluoro-5-imidazolyl)propanoic acid,
2-amino-3-(2-amino-5-imidazolyl)propanoic acid,
2-amino-3-(2-phenylaza-5-imidazolyl)propanoic acid,
2-amino-3-(1-methyl-2-nitro-5-imidazolyl)propanoic acid,
2-amino-3-(1-methyl4-nitro-5-imidazolyl)propanoic acid,
2-amino-3-(1-methyl-5-nitro-5-imidazolyl)propanoic acid,
2-amino-3-(2-mercapto-5-imidazolyl)propanoic acid,
2-amino-4-(5-imidazolyl)butanoic acid,
2-amino-3-(1-imidazolyl)propanoic acid,
2-amino-3-(2-imidazolyl)propanoic acid,

2-amino-(1-pyrazolyl)propanoic acid,
2-amino-(3-pyrazolyl)propanoic acid,
2-amino-(3,5-dialkyl-4-pyrazolyl)propanoic acid,
2-amino-3-(3-amino-1,2,4-triazol-1-yl)propanoic acid,
2-amino-3-(tetrazol-5-yl)propanoic acid,
2-amino-4-(5-tetrazolyl)butanoic acid,
2-amino-3-(6-methyl-3-indolyl)propanoic acid,
2-amino-3-(4-fluoro-3-indolyl)propanoic acid,
2-amino-3-(5-fluoro-3-indolyl)propanoic acid,
2-amino-3-(6-fluoro-3-indolyl)propanoic acid,
2-amino-3-(4,5,6,7-tetrafluoro-3-indolyl)propanoic acid,
2-amino-3-(5-chloro-3-indolyl)propanoic acid,
2-amino-3-(6-chloro-3-indolyl)propanoic acid,
2-amino-3-(7-chloro-3-indolyl)propanoic acid,
2-amino-3-(5-bromo-3-indolyl)propanoic acid,
2-amino-3-(7-bromo-3-indolyl)propanoic acid,
2-amino-3-(2-hydroxy-3-indolyl)propanoic acid,
2-amino-3-(5-hydroxy-3-indolyl)propanoic acid,
2-amino-3-(7-hydroxy-3-indolyl)propanoic acid,
2-amino-3-(2-alkylmercapto-3-indolyl)propanoic acid,
2-amino-3-(7-amino-3-indolyl)propanoic acid,
2-amino-3-(4-nitro-3-indolyl)propanoic acid,
2-amino-3-(7-nitro-3-indolyl)propanoic acid,
2-amino-3-(4-carboxy-3-indolyl)propanoic acid,
2-amino-3-(3-indolyl)butanoic acid,
2-amino-3-(2,3-dihydro-3-indolyl)propanoic acid,
2-amino-3-(2,3-dihydro-2-oxo-3-indolyl)propanoic acid,
2-amino-3-alkylmercapto-3-(3-indolyl)propanoic acid,
2-amino-3-(4-aza-3-indolyl)propanoic acid,
2-amino-3-(7-aza-3-indolyl)propanoic acid,
2-amino-3-(7-aza-6-chloro-4-methyl-3-indolyl)propanoic acid,
2-amino-3-(2,3-dihydrobenzofuran-3-yl)propanoic acid,
2-amino-3-(3-methyl-5-7-dialkylbenzofuran-2-yl)propanoic acid,
2-amino-3-(benzothiophen-3-yl)propanoic acid,
2-amino-3-(5-hydroxybenzothiophen-3-yl)propanoic acid,
2-amino-3-eoenzoselenol-3yl)propanoic acid,

2-amino-3-quinolylpropanoic acid,
2-amino-3-(8-hydroxy-5-quinolyl)propanoic acid,
2-amino-2-(5,6,7,8-tetrahydroquinol-5-yl)acetic acid,
2-amino-3-(3-coumarinyl)propanoic acid,
2-amino-2-(benzisoxazol-3-yl)acetic acid,
2-amino-2-(5-methylbenzisoxazol-3-yl)acetic acid,
2-amino-2-(6-methylbenzisoxazol-3-yl)acetic acid,
2-amino-2-(7-methylbenzisoxazol-3-yl)acetic acid,
2-amino-2-(5-bromobenzisoxazol-3-yl)acetic acid,
2-amino-3-(benzimidazol-2-yl)propanoic acid,
2-amino-3-(5,6-dichlorobenzimidazol-2-yl)propanoic acid,
2-amino-3-(5,6-dimethylbenzimidazol-2-yl)propanoic acid,
2-amino-3-(4,5,6,7-hydrobenzirnidazol-2-yl)propanoic acid,
2-amino-2-(benzimidazol-5-yl)acetic acid,
2-amino-2-(1,3-dihydro-2,2-dioxoisobenzothiophen-5-yl)acetic acid,
2-amino-2-(1,3-dihydro-2,2-dioxo-2,1,3-benzothiadiazol-5-yl)acetic acid,
2-amino-2-(2-oxobenzimidazol-5-yl)acetic acid,
2-amino-3-(4-hydroxybenzothiazol-6-yl)propanoic acid,
2-amino-3-(benzoxazol-2-yl)propanoic acid,
2-amino-3-(benzothiazol-2-yl)propanoic acid,
2-amino-3-(9-adeninyl)propanoic acid,
2-amino-2-(6-chloro-9-purinyl)acetic acid,
2-amino-2-(6-amino-9-purinyl)acetic acid,
2-amino-3-(6-purinyl)propanoic acid,
2-amino-3-(8-theobrominyl)propanoic acid,
2-amino-2-(1-uracilyl)acetic acid,
2-amino-2-(1-cytosinyl)acetic acid,
2-amino-3-(1-uracilyl)propanoic acid,
2-amino-3-(1-cytosinyl)propanoic acid,
2-amino-4-(1-pyrimidinyl)butanoic acid,
2-amino-4-(4-amino-1-pyrimidinyl)butanoic acid,
2-amino-4-(4-hydroxy-1-pyrimidinyl)butanoic acid,
2-amino-5-(1-pyrimidinyl)pentanoic acid,
2-amino-5-(4-amino-1-pyrimidinyl)pentanoic acid,
2-amino-5-(4-hydroxy-1-pyrimidinyl)pentanoic acid,
2-amino-3-(5-pyrimidinyl)propanoic acid,

2-amino-3-(6-uracilyl)propanoic acid,
2-amino-3-(2-pyrimidinyl)propanoic acid,
2-amino-3-(6-amino-4-chloro-2-pyrimidinyl)propanoic acid,
2-amino-3-(4-hydroxy-2-pyrimidinyl)propanoic acid,
2-amino-3-(2-amino-4-pyrimidinyl)propanoic acid,
2-amino-3-(4,5-dihydroxypyrimidin-2-yl)propanoic acid,
2-amino-3-(2-thiouracil-6-yl)propanoic acid,
2-amino-2-(5-alkyl-2-tetrahydrofuryl)acetic acid,
2-amino-2-(5-methyl-2,5-dihydro-2-furyl)acetic acid,
2-amino-2-(5-alkyl-2-furyl)acetic acid,
2-amino-2-(2-furyl)acetic acid,
2-amino-2-(3-hydroxy-5-methyl-4-isoxazolyl)acetic acid,
2-amino-3-(4-bromo-3-hydroxy-5-isoxazolyl)propanoic acid,
2-amino-3-(4-methyl-3-hydroxy-5-isoxazolyl)propanoic acid,
2-amino-3-(3-hydroxy-5-isoxazolyl)propanoic acid,
2-amino-2-(3-chloro-D2 -isoxazolin-5-yl)acetic acid,
2-amino-2-(3-oxo-5-isoxazolidinyl)acetic acid,
2-amino-3-(3,5-dioxo-1,2,4-oxadiazolin-2-yl)propanoic acid,
2-amino-3-(3-phenyl-5-isoxazolyl)propanoic acid,
2-amino-3-[3-(4-hydroxyphenyl)-1,2,4-oxadiazol-5-yl]propanoic acid,
2-amino-3-(2-thienyl)propanoic acid,
2-amino-2-(2-furyl)acetic acid,
2-amino-2-(2-thienyl)acetic acid,
2-amino-2-(2-thiazolyl)acetic acid,
2-amino-3-(2-thiazolyl)propanoic acid,
2-amino-4-(4-carboxy-2-thiazolyl)butanoic acid,
2-amino-3-(4-thiazolyl)propanoic acid,
2-amino-3-(2-selenolyl)propanoic acid,
2-amino-3-(2-amino-4-selenolyl)propanoic acid, and
2-amino-3-(beta-ribofuranosyl)propanoic acid.

[3] In a further preferred embodiment of the present invention

A is A^1, A^1-A^2, A^1-A^2-A^3, A^1-A^2-A^3-A^4, A^1-A^2-A^3-A^4-A^5, A^1-A^2-A^3-A^4-A^5-A^6, or A^1-A^2-A^3-A^4-A^5-A^6-A^7; and

A^1, A^2, A^3, A^4, A^5, A^6, and A^7 are independently selected from Ala, Arg, Asn, Asp, Aze, Cha, Cys, Dpa, Gln, Glu, Gly, His, Hyp, Ile, Irg, Leu, Lys, Met, Orn, Phe, Phe(4-fluoro), Pro, Sar, Ser, Thr, Trp, Tyr, Val, Asp(OMe), Glu(OMe), Hyp(OMe), Asp(O^tBu), Glu(O^tBu), Hyp(O^tBu), Thr(O^tBu), Asp(OBzl), Glu(OBzl), Hyp(OBzl), and Thr(OBzl).

[4] In a more preferred embodiment of the present invention

Y^1 and Y^2 are independently selected from:

a) -OH,

b) -F,

c) $-NR^{18}R^{19}$,

d) C_1-C_8 alkoxy, or

when taken together, Y^1 and Y^2 form:

e) a cyclic boron ester where said chain or ring contains from 2 to 20 carbon atoms, and, optionally, 1, 2, or 3 heteroatoms which can be N, S, or O,

f) a cyclic boron amide where said chain or ring contains from 2 to 20 carbon atoms and, optionally, 1, 2, or 3 heteroatoms which can be N, S, or O,

g) a cyclic boron amide-ester where said chain or ring contains from 2 to 20 carbon atoms and, optionally, 1, 2, or 3 heteroatoms which can be N, S, or O;

R^1 is selected from:

$-CH=CH_2$, $-CH_2CH=CH_2$, $-CH=CHCH_3$, -cyclopropyl, -cyclopropylmethyl, $-CH_2SR^{1A}$, $-CH_2(CH_3)SR^{1A}$, $-CH_2CO_2R^{1A}$, $-CF_2CF_3$, $-CF_2CF_2CF_3$, $-CH_2CH_2CF_3$, $-CF_2CHF_2$, $-CH_2CHF_2$, $-CH_2CH_2F$, and C_2-C_3 fluoroalkyl;

R^{1A} is H, methyl ,ethyl, propyl, phenyl, or $-CH_2$phenyl, wherein phenyl of R^{1A} is substituted with 0-3

substituents selected from $-CH_3$, $-CF_3$, $-NO_2$, -CN, -OH, -SH, $-OCH_3$, $-OCF_3$, -Cl, -Br, -I, and F;

A is A^1, A^1-A^2, A^1-A^2-A^3, A^1-A^2-A^3-A^4, A^1-A^2-A^3-A^4-A^5, or A^1-A^2-A^3-A^4-A^5-A^6;

A^1, A^2, A^3, A^4, A^5, and A^6 are independently selected from Ala, Arg, Asn, Asp, Aze, Cha, Cys, Dpa, Gln, Glu, Gly, His, Hyp, Ile, Irg, Leu, Lys, Met, Orn, Phe, Phe(4-fluoro), Pro, Sar, Ser, Thr, Trp, Tyr, Val, Asp(OMe), Glu(OMe), Hyp(OMe), Asp(O^tBu), Glu(O^tBu), Hyp(O^tBu), Thr(O^tBu), Asp(OBzl), Glu(OBzl), Hyp(OBzl), and Thr(OBzl);

R^2 is H, methyl, ethyl, propyl, or butyl;

R^3 is H, $-C(=O)-X-(CH_2)_m-Z$, C_1-C_4 alkyl, C_2-C_4 alkenyl, C_2-C_4 alkynyl, C_1-C_3 alkyl-R^4, C_2-C_4 alkenyl-R^4, C_2-C_4 alkynyl-R^4, $-C(=O)R^4$, $-CO_2R^4$, $-S(=O)R^4$, $-S(=O)_2R^4$, $-C(=O)NHR^4$, aryl, aryl(C_1-C_4 alkyl)-, wherein aryl is optionally substituted with 0-3 substituents selected from $-CH_3$, $-NO_2$, -CN, -OH, $-OCH_3$, $-SO_2CH_3$, $-CF_3$, -Cl, -Br, -I, and -F; or an NH_2-blocking group;

R^4 is C_1-C_4 alkyl substituted with 0-1 R^{4A},
C_3-C_6 cycloalkyl substituted with 0-3 R^{4B} and
aryl substituted with 0-3 R^{4B} and
5-14 membered heterocyclic ring system consisting of carbon atoms and 1-4 heteroatoms selected from the group: O, S, and N, and said heterocyclic ring system is substituted with 0-3 R^{4B};

R^{4A} is C_1-C_4 alkyl, halo, $-OR^{20}$, $-SR^{20}$, $-NR^{18}R^{19}$,
phenyl substituted with 0-3 R^{4B};
naphthyl substituted with 0-3 R^{4B};

benzyl substituted with 0-3 R^{4B}; or a
5-6 membered heterocyclic ring system containing 1, 2 or 3 heteroatoms selected from nitrogen, oxygen and sulfur; said heterocyclic ring system is substituted with 0-3 R^{4B};

R^{4B} is selected at each occurrence from the group:
H, F, Cl, Br, I, $-NO_2$, -CN, -NCS, $-CF_3$, $-OCF_3$, $-CH_3$, $-CH_2CH_3$, $-OCH_3$, =O, OH, $-CO_2H$, $-SCH_3$, $-SO_3H$, $-SO_2CH_3$, $-NH_2$, $-NH(CH_3)$, $-N(CH_3)_2$, phenyl, $-CO_2R^{21}$, $-C(=O)NR^{21}R^{21}$, $-NHC(=O)R^{21}$, $-NR^{21}R^{21}$, $-OR^{21a}$, $-SR^{21a}$, $-C(=O)R^{21a}$, $-S(=O)R^{21a}$, $-SO_2R^{21}$, $-SO_2NR^{21}R^{21}$, C_1-C_4 haloalkyl, C_1-C_4 haloalkoxy, C_1-C_4 thioalkoxy, C_1-C_4 alkyl substituted with 0-3 R^{4C}, C_1-C_4 alkoxy substituted with 0-3 R^{4C}, C_3-C_6 cycloalkyl substituted with 0-3 R^{4C}, aryl substituted with 0-5 R^{4C}, and aryl(C_1-C_4 alkyl)- substituted with 0-5 R^{4C}, and 5-6 membered heterocyclic ring system consisting of carbon atoms and 1-3 heteroatoms selected from the group: O, S, and N, and said heterocyclic ring system is substituted with 0-4 R^{4C};

R^{4C} is selected at each occurrence from the group:
H, F, Cl, Br, I, $-NO_2$, -CN, -NCS, $-CF_3$, $-OCF_3$, $-CH_3$, $-OCH_3$, =O, OH, $-CO_2H$, $-SO_2CH_3$, $-NH_2$, $-NH(CH_3)$, $-N(CH_3)_2$, phenyl, $-CO_2R^{21}$, $-C(=O)NR^{21}R^{21}$, $-NHC(=O)R^{21}$, $-NR^{21}R^{21}$, $-OR^{21a}$, $-SR^{21a}$, $-C(=O)R^{21a}$, $-S(=O)R^{21a}$, $-SO_2R^{21}$, $-SO_2NR^{21}R^{21}$, C_1-C_4 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, and C_1-C_4 haloalkoxy;

X is a bond,
C_1-C_4 alkyl substituted with 0-3 R^{11},
C_2-C_4 alkenyl substituted with 0-2 R^{11},
C_3-C_{10} carbocycle substituted with 0-2 R^{11},

C_6-C_{10} aryl substituted with 0-3 R^{11}, or

5-10 membered heterocyclic ring system consisting of carbon atoms and 1-4 heteroatoms selected from the group: O, S, and N, and said heterocyclic ring system is substituted with 0-2 R^{11};

R^{11} at each occurrence is independently selected from H, $-CH_3$, $-CH_2CH_3$, $-NO_2$, $-NH_2$, $-NH(CH_3)$, $-N(CH_3)_2$, $-SO_3H$, $-SO_2CH_3$, $-CO_2H$, $-CF_3$, $-OH$, $-OCH_3$, $-SCH_3$, $-OCF_3$, $-Cl$, $-Br$, $-I$, $-F$, $=O$, $-CN$, $-NCS$;

C_2-C_4 alkyl, C_2-C_4 alkoxy, C_2-C_4 thioalkoxy, C_1-C_4 haloalkyl, C_1-C_4 haloalkoxy, $-CO_2R^{21}$, $-C(=O)NR^{21}R^{21}$, $-NHC(=O)R^{21}$, $-NR^{21}R^{11}$, $-OR^{21a}$, $-SR^{21a}$, $-C(=O)R^{21a}$, $-S(=O)R^{21a}$, $-SO_2R^{21}$, $-SO_2NR^{21}R^{21}$, aryl, and aryl(C_1-C_4 alkyl)-, wherein aryl is optionally substituted with 0-3 substituents selected from $-CH_3$, $-NO_2$, $-CN$, $-OH$, $-OCH_3$, $-SO_2CH_3$, $-CF_3$, $-Cl$, $-Br$, $-I$, and F;

alternatively, two independent R^{11} groups may optionally be taken together to form $-(CH_2)_p-$;

m is 0, 1, 2, 3, or 4;

p is 1, 2, 3, or 4;

Z is selected from:

$-H$, $-R^{12}$, -halo, $-NHSO_2R^{12}$, $-SO_2NHR^{12}$, $-SO_2R^{12}$, $-C(=O)R^{12}$, $-OC(=O)C(=O)NHR^{12}$, $-NHC(=O)C(=O)OR^{12}$, $-OC(=O)R^{12}$, $-C(=O)OR^{12}$, $-OR^{12}$, $-SR^{12}$, and $-CN$;

R^{12} is H,

C_1-C_4 alkyl substituted with 0-3 R^{13},

C_3-C_{10} carbocycle substituted with 0-3 R^{13},

C_6-C_{10} aryl substituted with 0-3 R^{13}, or

5-10 membered heterocyclic ring system consisting of carbon atoms and 1-4 heteroatoms selected from the group: O, S, and N, and said heterocyclic ring system is substituted with 0-3 R^{13};

R^{13} at each occurrence is independently selected from H, $-CH_3$, $-CH_2CH_3$, $-NO_2$, $-SO_2OH$, $-SO_2CH_3$, CF_3, -Cl, -Br, -I, F, $-NH_2$, $-NH(CH_3)$, $-N(CH_3)_2$, $-NH(CH_2CH_3)$, $-N(CH_2CH_3)_2$, and C_1-C_4 alkyl;

R^{18} and R^{19} at each occurrence are independently selected from H, C_1-C_4 alkyl, aryl(C_1-C_4 alkyl)-, and C_3-C_7 cycloalkyl;

R^{20} is methyl, ethyl, propyl or butyl;

R^{21} is, at each occurrence, independently H or methyl, ethyl, propyl or butyl; and

R^{21a} is, at each occurrence, independently H, methyl, ethyl, propyl or butyl, phenyl, or C_1-C_4 haloalkyl.

[5] In an even more preferred embodiment of the present invention,

Y^1 and Y^2 are independently selected from:

a) -OH,

b) -F,

c) C_1-C_6 alkoxy, or

when taken together, Y^1 and Y^2 form:

d) a cyclic boron ester where said chain or ring contains from 2 to 16 carbon atoms, and, optionally, 1, 2, or 3 heteroatoms which can be N, S, or O,

R^1 is selected from:

$-CH=CH_2$, $-CH_2CH=CH_2$, -cyclopropyl, -cyclopropylmethyl, $-CF_2CF_3$, $-CH_2CH_2CF_3$, $-CH_2CHF_2$, and $-CH_2CH_2F$,

A is A^1, A^1-A^2, A^1-A^2-A^3, A^1-A^2-A^3-A^4, or A^1-A^2-A^3-A^4-A^5;

A^1, A^2, A^3, and A^4 are independently selected from Ala, Arg, Asn, Asp, Aze, Cha, Cys, Dpa, Gln, Glu, Gly, His, Hyp, Ile, Irg, Leu, Lys, Met, Orn, Phe, Phe(4-fluoro), Pro, Sar, Ser, Thr, Trp, Tyr, Val, Asp(OMe), Glu(OMe), Hyp(OMe), Asp(O^tBu), Glu(O^tBu), Hyp(O^tBu), Thr(O^tBu), Asp(OBzl), Glu(OBzl), Hyp(OBzl), and Thr(OBzl);

R^2 is H, methyl, or ethyl;

R^3 is H, $-C(=O)-X-(CH_2)_m-Z$, C_1-C_4 alkyl, C_2-C_4 alkenyl, C_2-C_4 alkynyl, $-C(=O)R^4$, $-CO_2R^4$, $-S(=O)R^4$, $-S(=O)_2R^4$, $-C(=O)NHR^4$, aryl, aryl(C_1-C_4 alkyl)-, wherein aryl is optionally substituted with 0-3 substituents selected from $-CH_3$, $-NO_2$, -CN, -OH, $-OCH_3$, $-SO_2CH_3$, $-CF_3$, -Cl, -Br, -I, and -F; or an NH_2-blocking group;

R^4 is C_1-C_4 alkyl substituted with 0-1 R^{4A},
C_3-C_6 cycloalkyl substituted with 0-3 R^{4B} and
aryl substituted with 0-3 R^{4B} and
5-14 membered heterocyclic ring system consisting of carbon atoms and 1-4 heteroatoms selected from the group: O, S, and N, and said heterocyclic ring system is substituted with 0-3 R^{4B};

R^{4A} is C_1-C_4 alkyl, halo, $-OR^{20}$, $-SR^{20}$, $-NR^{18}R^{19}$,
phenyl substituted with 0-3 R^{4B};
naphthyl substituted with 0-3 R^{4B};
benzyl substituted with 0-3 R^{4B}; or a
5-6 membered heterocyclic ring system containing 1, 2 or 3 heteroatoms selected from nitrogen, oxygen and

sulfur; said heterocyclic ring system is substituted with 0-3 R^{4B};

R^{4B} is selected at each occurrence from the group:
H, F, Cl, Br, I, $-NO_2$, -CN, -NCS, $-CF_3$, $-OCF_3$, $-CH_3$, $-CH_2CH_3$, $-OCH_3$, =O, OH, $-CO_2H$, $-SCH_3$, $-SO_3H$, $-SO_2CH_3$, $-NH_2$, $-NH(CH_3)$, $-N(CH_3)_2$, phenyl, $-CO_2R^{21}$, $-C(=O)NR^{21}R^{21}$, $-NHC(=O)R^{21}$, $-NR^{21}R^{21}$, $-OR^{21a}$, $-SR^{21a}$, $-C(=O)R^{21a}$, $-S(=O)R^{21a}$, $-SO_2R^{21}$, $-SO_2NR^{21}R^{21}$, C_1-C_4 haloalkyl, C_1-C_4 haloalkoxy, C_1-C_4 thioalkoxy, C_1-C_4 alkyl substituted with 0-3 R^{4C}, C_1-C_4 alkoxy substituted with 0-3 R^{4C}, C_3-C_6 cycloalkyl substituted with 0-3 R^{4C}, aryl substituted with 0-5 R^{4C}, and aryl(C_1-C_4 alkyl)- substituted with 0-5 R^{4C}, and 5-6 membered heterocyclic ring system consisting of carbon atoms and 1-3 heteroatoms selected from the group: O, S, and N, and said heterocyclic ring system is substituted with 0-4 R^{4C};

R^{4C} is selected at each occurrence from the group:
H, F, Cl, Br, I, $-NO_2$, -CN, -NCS, $-CF_3$, $-OCF_3$, $-CH_3$, $-OCH_3$, =O, OH, $-CO_2H$, $-SO_2CH_3$, $-NH_2$, $-NH(CH_3)$, $-N(CH_3)_2$, phenyl, $-CO_2R^{21}$, $-C(=O)NR^{21}R^{21}$, $-NHC(=O)R^{21}$, $-NR^{21}R^{21}$, $-OR^{21a}$, $-SR^{21a}$, $-C(=O)R^{21a}$, $-S(=O)R^{21a}$, $-SO_2R^{21}$, $-SO_2NR^{21}R^{21}$, C_1-C_4 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, and C_1-C_4 haloalkoxy;

X is a bond,
C_1-C_4 alkyl substituted with 0-3 R^{11},
C_2-C_4 alkenyl substituted with 0-2 R^{11},
C_3-C_{10} carbocycle substituted with 0-2 R^{11},
C_6-C_{10} aryl substituted with 0-3 R^{11}, or
5-10 membered heterocyclic ring system consisting of carbon atoms and 1-4 heteroatoms selected from

the group: O, S, and N, and said heterocyclic ring system is substituted with 0-2 R^{11};

R^{11} at each occurrence is independently selected from H, $-CH_3$, $-CH_2CH_3$, $-NO_2$, $-NH_2$, $-NH(CH_3)$, $-N(CH_3)_2$, $-SO_3H$, $-SO_2CH_3$, $-CO_2H$, $-CF_3$, $-OH$, $-OCH_3$, $-SCH_3$, $-OCF_3$, $-Cl$, $-Br$, $-I$, $-F$, $=O$, $-CN$, $-NCS$; C_2-C_4 alkyl, C_2-C_4 alkoxy, C_2-C_4 thioalkoxy, C_1-C_4 haloalkyl, C_1-C_4 haloalkoxy, $-CO_2R^{21}$, $-C(=O)NR^{21}R^{21}$, $-NHC(=O)R^{21}$, $-NR^{21}R^{11}$, $-OR^{21a}$, $-SR^{21a}$, $-C(=O)R^{21a}$, $-S(=O)R^{21a}$, $-SO_2R^{21}$, $-SO_2NR^{21}R^{21}$, aryl, and aryl(C_1-C_4 alkyl)-, wherein aryl is optionally substituted with 0-3 substituents selected from $-CH_3$, $-NO_2$, $-CN$, $-OH$, $-OCH_3$, $-SO_2CH_3$, $-CF_3$, $-Cl$, $-Br$, $-I$, and F;

alternatively, two independent R^{11} groups may optionally be taken together to form $-(CH_2)_p-$;

m is 0, 1, 2, or 3;

p is 1, 2, 3, or 4;

Z is selected from: -H, $-R^{12}$, -halo, $-NHSO_2R^{12}$, $-SO_2NHR^{12}$, $-SO_2R^{12}$, $-C(=O)R^{12}$, $-OC(=O)C(=O)NHR^{12}$, $-NHC(=O)C(=O)OR^{12}$, $-OC(=O)R^{12}$, $-C(=O)OR^{12}$, $-OR^{12}$, $-SR^{12}$, and $-CN$;

R^{12} is H, C_1-C_4 alkyl substituted with 0-3 R^{13}, C_3-C_{10} carbocycle substituted with 0-3 R^{13}, C_6-C_{10} aryl substituted with 0-3 R^{13}, or 5-10 membered heterocyclic ring system consisting of carbon atoms and 1-4 heteroatoms selected from the group: O, S, and N, and said heterocyclic ring system is substituted with 0-3 R^{13};

R^{13} at each occurrence is independently selected from H, $-CH_3$, $-CH_2CH_3$, $-NO_2$, $-SO_2OH$, $-SO_2CH_3$, CF_3, -Cl, -Br, -I, F, $-NH_2$, $-NH(CH_3)$, $-N(CH_3)_2$, $-NH(CH_2CH_3)$, $-N(CH_2CH_3)_2$, and C_1-C_4 alkyl;

R^{18} and R^{19} are independently selected from H, methyl, ethyl, propyl, butyl, benzyl, phenylethyl, cyclopropyl, cyclobutyl, cyclopentyl, and cyclohexyl; and

R^{20} is methyl, ethyl, propyl or butyl;

R^{21} is, at each occurrence, independently H or methyl, ethyl, propyl or butyl; and

R^{21a} is, at each occurrence, independently H, methyl, ethyl, propyl or butyl, phenyl, or C_1-C_4 haloalkyl.

[6] In another even more preferred embodiment of the present invention,

Y^1 and Y^2 are independently selected from:

a) -OH,

b) -F,

b) C_1-C_6 alkoxy, or

when taken together, Y^1 and Y^2 form:

c) a cyclic boron ester where said chain or ring contains from 2 to 12 carbon atoms, and, optionally, 1, 2, or 3 heteroatoms which can be N, S, or O,

R^1 is selected from $-CH_2CH_2CF_3$, $-CH_2CHF_2$, and $-CH_2CH_2F$,

A is A^1-A^2, A^1-A^2-A^3, or A^1-A^2-A^3-A^4;

A^1, A^2, A^3, and A^4 are independently selected from Ala,

Arg, Asn, Asp, Aze, Cha, Cys, Dpa, Gln, Glu, Gly, His, Hyp, Ile, Irg, Leu, Lys, Met, Orn, Phe, Phe(4-fluoro), Pro, Sar, Ser, Thr, Trp, Tyr, Val, Asp(OMe), Glu(OMe), Hyp(OMe), Asp(O^tBu), Glu(O^tBu), Hyp(O^tBu), Thr(O^tBu), Asp(OBzl), Glu(OBzl), Hyp(OBzl), and Thr(OBzl);

R^2 is H;

R^3 is H, methyl, ethyl, propyl, butyl, phenyl, benzyl, phenylethyl-, phenylpropyl-, phenylbutyl-, $-C(=O)R^4$, $-S(=O)_2R^4$, $-C(=O)-X-(CH_2)_m-Z$, or an NH_2-blocking group;

R^4 is C_1-C_4 alkyl substituted with 0-1 R^{4A},
C_3-C_6 cycloalkyl substituted with 0-3 R^{4B} and
aryl substituted with 0-2 R^{4B} and
5-10 membered heterocyclic ring system consisting of carbon atoms and 1-4 heteroatoms selected from the group: O, S, and N, and said heterocyclic ring system is substituted with 0-2 R^{4B};

R^{4A} is C_1-C_4 alkyl, halo, $-OR^{20}$, $-SR^{20}$, $-NR^{18}R^{19}$,
phenyl substituted with 0-3 R^{4B};
naphthyl substituted with 0-3 R^{4B};
benzyl substituted with 0-3 R^{4B}; or a
5-6 membered heterocyclic ring system containing 1, 2 or 3 heteroatoms selected from nitrogen, oxygen and sulfur; said heterocyclic ring system is substituted with 0-3 R^{4B};

R^{4B} is selected at each occurrence from the group:
H, F, Cl, Br, I, $-NO_2$, $-CF_3$, $-OCF_3$, $-CH_3$, $-CH_2CH_3$, $-OCH_3$, =O, -OH, $-CO_2H$, $-SCH_3$, $-SO_3H$, $-SO_2CH_3$, $-NH_2$, $-NH(CH_3)$, $-N(CH_3)_2$, propyl, butyl, ethoxy, propoxy, butoxy, thioethoxy, thiopropoxy, thiobutoxy, cyclopropyl, cyclobutyl,
phenyl substituted with 0-3 R^{4C};

phenyl(C_1-C_4 alkyl)- substituted with 0-3 R^{4C}, and
5-6 membered heterocyclic ring system consisting of carbon atoms and 1-3 heteroatoms selected from the group: O, S, and N, and said heterocyclic ring system is substituted with 0-3 R^{4C};

R^{4C} is selected at each occurrence from the group: H, F, Cl, Br, I, $-NO_2$, -CN, $-CF_3$, $-OCF_3$, $-CH_3$, $-OCH_3$, OH, and $-SO_2CH_3$;

X is a bond,
C_1-C_4 alkyl substituted with 0-3 R^{11},
C_2-C_4 alkenyl substituted with 0-2 R^{11},
C_3-C_{10} carbocycle substituted with 0-2 R^{11}, wherein the carbocycle is selected from cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, adamantanyl, norbornanyl, norbornenyl, and fluorenyl,
phenyl substituted with 0-3 R^{11},
naphthyl substituted with 0-3 R^{11},
C_5-C_{10} heterocycle substituted with 0-2 R^{11}, wherein the heterocycle is selected from furanyl, oxazolyl, isoxazolyl, benzthiophenyl, pyrrolidinyl, pyrrolyl, carbazolyl, pyridinyl, thiophenyl, triazolyl, thiadiazolyl, benzodioxanyl, benzodioxolyl, quinazolinyl, quinoxalinyl, and quinolinyl;

R^{11} at each occurrence is independently selected from H, $-CH_3$, $-CH_2CH_3$, $-NO_2$, $-NH_2$, $-SO_3H$, $-SO_2CH_3$, $-CO_2H$, $-CF_3$, -OH, $-OCH_3$, $-SCH_3$, $-OCF_3$, -Cl, -Br, -I, -F, =O, C_1-C_4 alkyl, C_1-C_4 alkoxy, C_1-C_4 thioalkoxy, phenyl, and phenyl(C_1-C_4 alkyl)-, wherein phenyl is optionally substituted with 0-3 substituents selected from $-CH_3$, $-NO_2$, -CN, -OH, $-OCH_3$, $-OCF_3$, $-SO_2CH_3$, $-CF_3$, -Cl, -Br, -I, and F;

alternatively, two independent R^{11} groups may optionally be taken together to form $-(CH_2)_p-$;

m is 0, 1, or 2;

p is 2, 3, or 4;

Z is selected from:
-H, $-R^{12}$, -halo, $-NHSO_2R^{12}$, $-SO_2NHR^{12}$, $-SO_2R^{12}$, $-C(=O)R^{12}$, $-OC(=O)C(=O)NHR^{12}$, $-NHC(=O)C(=O)OR^{12}$, $-OC(=O)R^{12}$, $-C(=O)OR^{12}$, $-OR^{12}$, $-SR^{12}$, and -CN;

R^{12} is H,
C_1-C_4 alkyl substituted with 0-3 R^{13},
C_3-C_{10} carbocycle substituted with 0-3 R^{13},
phenyl substituted with 0-3 R^{13}, or
C_5-C_{10} heterocycle substituted with 0-3 R^{13}; wherein the heterocycle is selected from furanyl, oxazolyl, isoxazolyl, pyrrolidinyl, pyrrolyl, pyridinyl, thiophenyl, triazolyl, and thiadiazolyl;

R^{13} at each occurrence is independently selected from H, $-CH_3$, $-CH_2CH_3$, $-NO_2$, $-SO_2OH$, $-SO_2CH_3$, $-CF_3$, -Cl, -Br, -I, -F, $-NH_2$, $-NH(CH_3)$, $-N(CH_3)_2$, $-NH(CH_2CH_3)$, $-N(CH_2CH_3)_2$, methyl, ethyl, propyl, and butyl;

R^{18} and R^{19} are independently selected from H, methyl, ethyl, propyl, butyl, benzyl, phenylethyl, cyclopropyl, cyclobutyl, cyclopentyl, and cyclohexyl; and

R^{20} is methyl, ethyl, propyl or butyl.

[7] In another even more preferred embodiment of the present invention,

Y^1 and Y^2 are independently selected from:

a) -OH,

b) -F,

b) C_1-C_6 alkoxy, or

when taken together, Y^1 and Y^2 form:

c) a cyclic boron ester where said chain or ring contains from 2 to 12 carbon atoms, and, optionally, 1, 2, or 3 heteroatoms which can be N, S, or O,

R^1 is $-CH_2CHF_2$;

A is A^1-A^2, A^1-A^2-A^3, or A^1-A^2-A^3-A^4;

A^1, A^2, A^3, and A^4 are independently selected from Ala, Arg, Asn, Asp, Aze, Cha, Cys, Dpa, Gln, Glu, Gly, His, Hyp, Ile, Irg, Leu, Lys, Met, Orn, Phe, Phe(4-fluoro), Pro, Sar, Ser, Thr, Trp, Tyr, Val, Asp(OMe), Glu(OMe), Hyp(OMe), Asp(O^tBu), Glu(O^tBu), Hyp(O^tBu), Thr(O^tBu), Asp(OBzl), Glu(OBzl), Hyp(OBzl), and Thr(OBzl);

R^2 is H;

R^3 is H, methyl, ethyl, propyl, butyl, phenyl, benzyl, phenylethyl-, phenylpropyl-, phenylbutyl-, $-C(=O)R^4$, $-S(=O)_2R^4$, $-C(=O)-X-(CH_2)_m-Z$, or an NH_2-blocking group;

R^4 is C_1-C_4 alkyl substituted with 0-1 R^{4A},

C_3-C_6 cycloalkyl substituted with 0-3 R^{4B} and

aryl substituted with 0-2 R^{4B} and

5-10 membered heterocyclic ring system consisting of carbon atoms and 1-4 heteroatoms selected from the group: O, S, and N, and said heterocyclic ring system is substituted with 0-2 R^{4B};

R^{4A} is C_1-C_4 alkyl, halo, $-OR^{20}$, $-SR^{20}$, $-NR^{18}R^{19}$,

phenyl substituted with 0-3 R^{4B};
naphthyl substituted with 0-3 R^{4B};
benzyl substituted with 0-3 R^{4B}; or a
5-6 membered heterocyclic ring system containing 1, 2 or 3 heteroatoms selected from nitrogen, oxygen and sulfur; said heterocyclic ring system is substituted with 0-3 R^{4B};

R^{4B} is selected at each occurrence from the group:
H, F, Cl, Br, I, $-NO_2$, $-CF_3$, $-OCF_3$, $-CH_3$, $-CH_2CH_3$, $-OCH_3$, =O, -OH, $-CO_2H$, $-SCH_3$, $-SO_3H$, $-SO_2CH_3$, $-NH_2$, $-NH(CH_3)$, $-N(CH_3)_2$, propyl, butyl, ethoxy, propoxy, butoxy, thioethoxy, thiopropoxy, thiobutoxy, cyclopropyl, cyclobutyl,
phenyl substituted with 0-3 R^{4C};
phenyl(C_1-C_4 alkyl)- substituted with 0-3 R^{4C}, and
5-6 membered heterocyclic ring system consisting of carbon atoms and 1-3 heteroatoms selected from the group: O, S, and N, and said heterocyclic ring system is substituted with 0-3 R^{4C};

R^{4C} is selected at each occurrence from the group:
H, F, Cl, Br, I, $-NO_2$, -CN, $-CF_3$, $-OCF_3$, $-CH_3$, $-OCH_3$, OH, and $-SO_2CH_3$;

X is a bond,
C_1-C_4 alkyl substituted with 0-3 R^{11},
C_2-C_4 alkenyl substituted with 0-2 R^{11},
C_3-C_{10} carbocycle substituted with 0-2 R^{11}, wherein the carbocycle is selected from cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, adamantanyl, norbornanyl, norbornenyl, and fluorenyl,
phenyl substituted with 0-3 R^{11},
naphthyl substituted with 0-3 R^{11},
C_5-C_{10} heterocycle substituted with 0-2 R^{11}, wherein the heterocycle is selected from furanyl,

oxazolyl, isoxazolyl, benzthiophenyl, pyrrolidinyl, pyrrolyl, carbazolyl, pyridinyl, thiophenyl, triazolyl, thiadiazolyl, benzodioxanyl, benzodioxolyl, quinazolinyl, quinoxalinyl, and quinolinyl;

R^{11} at each occurrence is independently selected from H, $-CH_3$, $-CH_2CH_3$, $-NO_2$, $-NH_2$, $-SO_3H$, $-SO_2CH_3$, $-CO_2H$, $-CF_3$, $-OH$, $-OCH_3$, $-SCH_3$, $-OCF_3$, $-Cl$, $-Br$, $-I$, $-F$, =O, C_1-C_4 alkyl, C_1-C_4 alkoxy, C_1-C_4 thioalkoxy, phenyl, and phenyl(C_1-C_4 alkyl)-, wherein phenyl is optionally substituted with 0-3 substituents selected from $-CH_3$, $-NO_2$, $-CN$, $-OH$, $-OCH_3$, $-OCF_3$, $-SO_2CH_3$, $-CF_3$, $-Cl$, $-Br$, $-I$, and F;

alternatively, two independent R^{11} groups may optionally be taken together to form $-(CH_2)_p-$;

m is 0, 1, or 2;

p is 2, 3, or 4;

Z is selected from:
$-H$, $-R^{12}$, -halo, $-NHSO_2R^{12}$, $-SO_2NHR^{12}$, $-SO_2R^{12}$, $-C(=O)R^{12}$, $-OC(=O)C(=O)NHR^{12}$, $-NHC(=O)C(=O)OR^{12}$, $-OC(=O)R^{12}$, $-C(=O)OR^{12}$, $-OR^{12}$, $-SR^{12}$, and $-CN$;

R^{12} is H,
C_1-C_4 alkyl substituted with 0-3 R^{13},
C_3-C_{10} carbocycle substituted with 0-3 R^{13},
phenyl substituted with 0-3 R^{13}, or
C_5-C_{10} heterocycle substituted with 0-3 R^{13}; wherein the heterocycle is selected from furanyl, oxazolyl, isoxazolyl, pyrrolidinyl, pyrrolyl, pyridinyl, thiophenyl, triazolyl, and thiadiazolyl;

R^{13} at each occurrence is independently selected from H, $-CH_3$, $-CH_2CH_3$, $-NO_2$, $-SO_2OH$, $-SO_2CH_3$, $-CF_3$, -Cl, -Br, -I, -F, $-NH_2$, $-NH(CH_3)$, $-N(CH_3)_2$, $-NH(CH_2CH_3)$, $-N(CH_2CH_3)_2$, methyl, ethyl, propyl, and butyl;

R^{18} and R^{19} are independently selected from H, methyl, ethyl, propyl, butyl, benzyl, phenylethyl, cyclopropyl, cyclobutyl, cyclopentyl, and cyclohexyl; and

R^{20} is methyl, ethyl, propyl or butyl.

[8] In a second embodiment the present invention provides a compound of Formula (I) or a pharmaceutically acceptable salt form thereof, wherein:

Y^1 and Y^2 are independently selected from:

a) -OH,

b) -F,

c) $-NR^{18}R^{19}$,

d) C_1-C_8 alkoxy, or

when taken together, Y^1 and Y^2 form:

e) a cyclic boron ester where said chain or ring contains from 2 to 20 carbon atoms, and, optionally, 1, 2, or 3 heteroatoms which can be N, S, or O,

f) a cyclic boron amide where said chain or ring contains from 2 to 20 carbon atoms and, optionally, 1, 2, or 3 heteroatoms which can be N, S, or O,

g) a cyclic boron amide-ester where said chain or ring contains from 2 to 20 carbon atoms and, optionally, 1, 2, or 3 heteroatoms which can be N, S, or O;

R^1 is selected from:

$-CH=CH_2$, $-CH_2CH=CH_2$, $-CH=CHCH_3$, -cyclopropyl, -cyclopropylmethyl, $-CH_2SR^{1A}$, $-CH_2(CH_3)SR^{1A}$, $-CH_2CO_2R^{1A}$,

$-CF_2CF_3$, $-CF_2CF_2CF_3$, $-CH_2CH_2CF_3$, $-CF_2CHF_2$, $-CH_2CHF_2$, $-CH_2CH_2F$, and C_2-C_3 fluoroalkyl;

R^{1A} is H, methyl ,ethyl, propyl, phenyl, or $-CH_2$phenyl, wherein phenyl of R^{1A} is substituted with 0-3 substituents selected from $-CH_3$, $-CF_3$, $-NO_2$, -CN, -OH, -SH, $-OCH_3$, $-OCF_3$, -Cl, -Br, -I, and F;

A is A^1, A^1-A^2, A^1-A^2-A^3, A^1-A^2-A^3-A^4, A^1-A^2-A^3-A^4-A^5, or A^1-A^2-A^3-A^4-A^5-A^6;

A^1, A^2, A^3, A^4, A^5, and A^6 are independently selected from Ala, Arg, Asn, Asp, Aze, Cha, Cys, Dpa, Gln, Glu, Gly, His, Hyp, Ile, Irg, Leu, Lys, Met, Orn, Phe, Phe(4-fluoro), Pro, Sar, Ser, Thr, Trp, Tyr, Val, Asp(OMe), Glu(OMe), Hyp(OMe), Asp(O^tBu), Glu(O^tBu), Hyp(O^tBu), Thr(O^tBu), Asp(OBzl), Glu(OBzl), Hyp(OBzl), and Thr(OBzl);

R^2 is H, methyl, ethyl, propyl, or butyl;

R^3 is H, $-C(=O)-X-(CH_2)_m-Z$, C_1-C_4 alkyl, C_2-C_4 alkenyl, C_2-C_4 alkynyl, C_1-C_3 alkyl-R^4, C_2-C_4 alkenyl-R^4, C_2-C_4 alkynyl-R^4, $-C(=O)R^4$, $-CO_2R^4$, $-S(=O)R^4$, $-S(=O)_2R^4$, $-C(=O)NHR^4$, aryl, aryl(C_1-C_4 alkyl)-, wherein aryl is optionally substituted with 0-3 substituents selected from $-CH_3$, $-NO_2$, -CN, -OH, $-OCH_3$, $-SO_2CH_3$, $-CF_3$, -Cl, -Br, -I, and -F; or an NH_2-blocking group;

R^4 is C_1-C_4 alkyl substituted with 0-1 R^{4A},
C_3-C_6 cycloalkyl substituted with 0-3 R^{4B} and
aryl substituted with 0-3 R^{4B} and
5-14 membered heterocyclic ring system consisting of carbon atoms and 1-4 heteroatoms selected from

the group: O, S, and N, and said heterocyclic ring system is substituted with 0-3 R^{4B};

R^{4A} is C_1-C_4 alkyl, halo, $-OR^{20}$, $-SR^{20}$, $-NR^{18}R^{19}$,
phenyl substituted with 0-3 R^{4B};
naphthyl substituted with 0-3 R^{4B};
benzyl substituted with 0-3 R^{4B}; or a
5-6 membered heterocyclic ring system containing 1, 2 or 3 heteroatoms selected from nitrogen, oxygen and sulfur; said heterocyclic ring system is substituted with 0-3 R^{4B};

R^{4B} is selected at each occurrence from the group:
H, F, Cl, Br, I, $-NO_2$, -CN, -NCS, $-CF_3$, $-OCF_3$, $-CH_3$, $-CH_2CH_3$, $-OCH_3$, =O, OH, $-CO_2H$, $-SCH_3$, $-SO_3H$, $-SO_2CH_3$, $-NH_2$, $-NH(CH_3)$, $-N(CH_3)_2$, phenyl, $-CO_2R^{21}$, $-C(=O)NR^{21}R^{21}$, $-NHC(=O)R^{21}$, $-NR^{21}R^{21}$, $-OR^{21a}$, $-SR^{21a}$, $-C(=O)R^{21a}$, $-S(=O)R^{21a}$, $-SO_2R^{21}$, $-SO_2NR^{21}R^{21}$, C_1-C_4 haloalkyl, C_1-C_4 haloalkoxy, C_1-C_4 thioalkoxy, C_1-C_4 alkyl substituted with 0-3 R^{4C}, C_1-C_4 alkoxy substituted with 0-3 R^{4C}, C_3-C_6 cycloalkyl substituted with 0-3 R^{4C}, aryl substituted with 0-5 R^{4C}, and aryl(C_1-C_4 alkyl)- substituted with 0-5 R^{4C}, and
5-6 membered heterocyclic ring system consisting of carbon atoms and 1-3 heteroatoms selected from the group: O, S, and N, and said heterocyclic ring system is substituted with 0-4 R^{4C};

R^{4C} is selected at each occurrence from the group:
H, F, Cl, Br, I, $-NO_2$, -CN, -NCS, $-CF_3$, $-OCF_3$, $-CH_3$, $-OCH_3$, =O, OH, $-CO_2H$, $-SO_2CH_3$, $-NH_2$, $-NH(CH_3)$, $-N(CH_3)_2$, phenyl, $-CO_2R^{21}$, $-C(=O)NR^{21}R^{21}$, $-NHC(=O)R^{21}$, $-NR^{21}R^{21}$, $-OR^{21a}$, $-SR^{21a}$, $-C(=O)R^{21a}$, $-S(=O)R^{21a}$,

$-SO_2R^{21}$, $-SO_2NR^{21}R^{21}$, C_1-C_4 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, and C_1-C_4 haloalkoxy;

X is a bond,
C_1-C_4 alkyl substituted with 0-3 R^{11},
C_2-C_4 alkenyl substituted with 0-2 R^{11},
C_3-C_{10} carbocycle substituted with 0-2 R^{11},
C_6-C_{10} aryl substituted with 0-3 R^{11}, or
5-10 membered heterocyclic ring system consisting of carbon atoms and 1-4 heteroatoms selected from the group: O, S, and N, and said heterocyclic ring system is substituted with 0-2 R^{11};

R^{11} at each occurrence is independently selected from
H, $-CH_3$, $-CH_2CH_3$, $-NO_2$, $-NH_2$, $-NH(CH_3)$, $-N(CH_3)_2$, $-SO_3H$, $-SO_2CH_3$, $-CO_2H$, $-CF_3$, $-OH$, $-OCH_3$, $-SCH_3$, $-OCF_3$, $-Cl$, $-Br$, $-I$, $-F$, $=O$, $-CN$, $-NCS$;
C_2-C_4 alkyl, C_2-C_4 alkoxy, C_2-C_4 thioalkoxy, C_1-C_4 haloalkyl, C_1-C_4 haloalkoxy, $-CO_2R^{21}$, $-C(=O)NR^{21}R^{21}$, $-NHC(=O)R^{21}$, $-NR^{21}R^{11}$, $-OR^{21a}$, $-SR^{21a}$, $-C(=O)R^{21a}$, $-S(=O)R^{21a}$, $-SO_2R^{21}$, $-SO_2NR^{21}R^{21}$, aryl, and aryl(C_1-C_4 alkyl)-, wherein aryl is optionally substituted with 0-3 substituents selected from $-CH_3$, $-NO_2$, $-CN$, $-OH$, $-OCH_3$, $-SO_2CH_3$, $-CF_3$, $-Cl$, $-Br$, $-I$, and F;

alternatively, two independent R^{11} groups may optionally be taken together to form $-(CH_2)_p-$;

m is 0, 1, 2, 3, or 4;

p is 1, 2, 3, or 4;

Z is selected from:
$-H$, $-R^{12}$, -halo, $-NHSO_2R^{12}$, $-SO_2NHR^{12}$, $-SO_2R^{12}$,

$-C(=O)R^{12}$, $-OC(=O)C(=O)NHR^{12}$, $-NHC(=O)C(=O)OR^{12}$, $-OC(=O)R^{12}$, $-C(=O)OR^{12}$, $-OR^{12}$, $-SR^{12}$, and -CN;

R^{12} is H,
C_1-C_4 alkyl substituted with 0-3 R^{13},
C_3-C_{10} carbocycle substituted with 0-3 R^{13},
C_6-C_{10} aryl substituted with 0-3 R^{13}, or
5-10 membered heterocyclic ring system consisting of carbon atoms and 1-4 heteroatoms selected from the group: O, S, and N, and said heterocyclic ring system is substituted with 0-3 R^{13};

R^{13} at each occurrence is independently selected from H, $-CH_3$, $-CH_2CH_3$, $-NO_2$, $-SO_2OH$, $-SO_2CH_3$, CF_3, -Cl, -Br, -I, F, $-NH_2$, $-NH(CH_3)$, $-N(CH_3)_2$, $-NH(CH_2CH_3)$, $-N(CH_2CH_3)_2$, and C_1-C_4 alkyl;

R^{18} and R^{19} at each occurrence are independently selected from H, C_1-C_4 alkyl, aryl(C_1-C_4 alkyl)-, and C_3-C_7 cycloalkyl;

R^{20} is methyl, ethyl, propyl or butyl;

R^{21} is, at each occurrence, independently H or methyl, ethyl, propyl or butyl; and

R^{21a} is, at each occurrence, independently H, methyl, ethyl, propyl or butyl, phenyl, or C_1-C_4 haloalkyl;

provided when R^1 is $-CH_2CH_2F$, the A is not -Gly-Pro-;
provided when R^1 is $-CH_2CH=CH_2$, then A is not
-Asp-Glu-(2-methyl-Phe)-(3-methyl-Val)-Leu-,
-Asp-Glu-(2-methyl-Phe)-(3-methyl-Val)-(cyclopentyl-Ala)-,
-Asp-Glu-(2-methyl-Phe)-(cyclohexyl-Ala)-Leu-,
-Asp-Glu-(2-methyl-Phe)-(phenyl-Gly)-Leu-,
-Asp-Glu-(2-methyl-Phe)-(cyclohexyl-Ala)-Leu-,

-Asp-Glu-(2-methyl-Phe)-(3-methyl-Val)-(Pro)-,
-Asp-Glu-(2-methyl-Phe)-Phe-Leu-, or
-Asp-Glu-(4-chloro-2-methyl-Phe)-(3-methyl-Val)-(Leu)-.

[9] In a more preferred second embodiment of the present invention,

Y^1 and Y^2 are independently selected from:

a) -OH,

b) -F,

c) C_1-C_6 alkoxy, or

when taken together, Y^1 and Y^2 form:

d) a cyclic boron ester where said chain or ring contains from 2 to 16 carbon atoms, and, optionally, 1, 2, or 3 heteroatoms which can be N, S, or O,

R^1 is selected from:

$-CH=CH_2$, $-CH_2CH=CH_2$, -cyclopropyl, -cyclopropylmethyl, $-CF_2CF_3$, $-CH_2CH_2CF_3$, $-CH_2CHF_2$, and $-CH_2CH_2F$,

A is A^1, A^1-A^2, A^1-A^2-A^3, A^1-A^2-A^3-A^4, or A^1-A^2-A^3-A^4-A^5;

A^1, A^2, A^3, and A^4 are independently selected from Ala, Arg, Asn, Asp, Aze, Cha, Cys, Dpa, Gln, Glu, Gly, His, Hyp, Ile, Irg, Leu, Lys, Met, Orn, Phe, Phe(4-fluoro), Pro, Sar, Ser, Thr, Trp, Tyr, Val, Asp(OMe), Glu(OMe), Hyp(OMe), Asp(O^tBu), Glu(O^tBu), Hyp(O^tBu), Thr(O^tBu), Asp(OBzl), Glu(OBzl), Hyp(OBzl), and Thr(OBzl);

R^2 is H, methyl, or ethyl;

R^3 is H, $-C(=O)-X-(CH_2)_m-Z$, C_1-C_4 alkyl, C_2-C_4 alkenyl, C_2-C_4 alkynyl, $-C(=O)R^4$, $-CO_2R^4$, $-S(=O)R^4$, $-S(=O)_2R^4$, $-C(=O)NHR^4$, aryl, aryl(C_1-C_4 alkyl)-, wherein aryl is optionally substituted with 0-3 substituents selected

from $-CH_3$, $-NO_2$, -CN, -OH, $-OCH_3$, $-SO_2CH_3$, $-CF_3$, -Cl, -Br, -I, and -F; or an NH_2-blocking group;

R^4 is C_1-C_4 alkyl substituted with 0-1 R^{4A},
C_3-C_6 cycloalkyl substituted with 0-3 R^{4B} and
aryl substituted with 0-3 R^{4B} and
5-14 membered heterocyclic ring system consisting of carbon atoms and 1-4 heteroatoms selected from the group: O, S, and N, and said heterocyclic ring system is substituted with 0-3 R^{4B};

R^{4A} is C_1-C_4 alkyl, halo, $-OR^{20}$, $-SR^{20}$, $-NR^{18}R^{19}$,
phenyl substituted with 0-3 R^{4B};
naphthyl substituted with 0-3 R^{4B};
benzyl substituted with 0-3 R^{4B}; or a
5-6 membered heterocyclic ring system containing 1, 2 or 3 heteroatoms selected from nitrogen, oxygen and sulfur; said heterocyclic ring system is substituted with 0-3 R^{4B};

R^{4B} is selected at each occurrence from the group:
H, F, Cl, Br, I, $-NO_2$, -CN, -NCS, $-CF_3$, $-OCF_3$, $-CH_3$, $-CH_2CH_3$, $-OCH_3$, =O, OH, $-CO_2H$, $-SCH_3$, $-SO_3H$, $-SO_2CH_3$, $-NH_2$, $-NH(CH_3)$, $-N(CH_3)_2$, phenyl, $-CO_2R^{21}$, $-C(=O)NR^{21}R^{21}$, $-NHC(=O)R^{21}$, $-NR^{21}R^{21}$, $-OR^{21a}$, $-SR^{21a}$, $-C(=O)R^{21a}$, $-S(=O)R^{21a}$, $-SO_2R^{21}$, $-SO_2NR^{21}R^{21}$, C_1-C_4 haloalkyl, C_1-C_4 haloalkoxy, C_1-C_4 thioalkoxy, C_1-C_4 alkyl substituted with 0-3 R^{4C}, C_1-C_4 alkoxy substituted with 0-3 R^{4C}, C_3-C_6 cycloalkyl substituted with 0-3 R^{4C}, aryl substituted with 0-5 R^{4C}, and aryl(C_1-C_4 alkyl)- substituted with 0-5 R^{4C}, and
5-6 membered heterocyclic ring system consisting of carbon atoms and 1-3 heteroatoms selected from

the group: O, S, and N, and said heterocyclic ring system is substituted with 0-4 R^{4C};

R^{4C} is selected at each occurrence from the group: H, F, Cl, Br, I, $-NO_2$, -CN, -NCS, $-CF_3$, $-OCF_3$, $-CH_3$, $-OCH_3$, =O, OH, $-CO_2H$, $-SO_2CH_3$, $-NH_2$, $-NH(CH_3)$, $-N(CH_3)_2$, phenyl, $-CO_2R^{21}$, $-C(=O)NR^{21}R^{21}$, $-NHC(=O)R^{21}$, $-NR^{21}R^{21}$, $-OR^{21a}$, $-SR^{21a}$, $-C(=O)R^{21a}$, $-S(=O)R^{21a}$, $-SO_2R^{21}$, $-SO_2NR^{21}R^{21}$, C_1-C_4 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, and C_1-C_4 haloalkoxy;

X is a bond,
C_1-C_4 alkyl substituted with 0-3 R^{11},
C_2-C_4 alkenyl substituted with 0-2 R^{11},
C_3-C_{10} carbocycle substituted with 0-2 R^{11},
C_6-C_{10} aryl substituted with 0-3 R^{11}, or
5-10 membered heterocyclic ring system consisting of carbon atoms and 1-4 heteroatoms selected from the group: O, S, and N, and said heterocyclic ring system is substituted with 0-2 R^{11};

R^{11} at each occurrence is independently selected from H, $-CH_3$, $-CH_2CH_3$, $-NO_2$, $-NH_2$, $-NH(CH_3)$, $-N(CH_3)_2$, $-SO_3H$, $-SO_2CH_3$, $-CO_2H$, $-CF_3$, -OH, $-OCH_3$, $-SCH_3$, $-OCF_3$, -Cl, -Br, -I, -F, =O, -CN, -NCS;
C_2-C_4 alkyl, C_2-C_4 alkoxy, C_2-C_4 thioalkoxy, C_1-C_4 haloalkyl, C_1-C_4 haloalkoxy, $-CO_2R^{21}$, $-C(=O)NR^{21}R^{21}$, $-NHC(=O)R^{21}$, $-NR^{21}R^{11}$, $-OR^{21a}$, $-SR^{21a}$, $-C(=O)R^{21a}$, $-S(=O)R^{21a}$, $-SO_2R^{21}$, $-SO_2NR^{21}R^{21}$, aryl, and aryl(C_1-C_4 alkyl)-, wherein aryl is optionally substituted with 0-3 substituents selected from $-CH_3$, $-NO_2$, -CN, -OH, $-OCH_3$, $-SO_2CH_3$, $-CF_3$, -Cl, -Br, -I, and F;

alternatively, two independent R^{11} groups may optionally be taken together to form $-(CH_2)_p-$;

m is 0, 1, 2, or 3;

p is 1, 2, 3, or 4;

Z is selected from:
$-H$, $-R^{12}$, -halo, $-NHSO_2R^{12}$, $-SO_2NHR^{12}$, $-SO_2R^{12}$, $-C(=O)R^{12}$, $-OC(=O)C(=O)NHR^{12}$, $-NHC(=O)C(=O)OR^{12}$, $-OC(=O)R^{12}$, $-C(=O)OR^{12}$, $-OR^{12}$, $-SR^{12}$, and $-CN$;

R^{12} is H,
C_1-C_4 alkyl substituted with 0-3 R^{13},
C_3-C_{10} carbocycle substituted with 0-3 R^{13},
C_6-C_{10} aryl substituted with 0-3 R^{13}, or
5-10 membered heterocyclic ring system consisting of carbon atoms and 1-4 heteroatoms selected from the group: O, S, and N, and said heterocyclic ring system is substituted with 0-3 R^{13};

R^{13} at each occurrence is independently selected from H, $-CH_3$, $-CH_2CH_3$, $-NO_2$, $-SO_2OH$, $-SO_2CH_3$, CF_3, -Cl, -Br, -I, F, $-NH_2$, $-NH(CH_3)$, $-N(CH_3)_2$, $-NH(CH_2CH_3)$, $-N(CH_2CH_3)_2$, and C_1-C_4 alkyl;

R^{18} and R^{19} are independently selected from H, methyl, ethyl, propyl, butyl, benzyl, phenylethyl, cyclopropyl, cyclobutyl, cyclopentyl, and cyclohexyl; and

R^{20} is methyl, ethyl, propyl or butyl;

R^{21} is, at each occurrence, independently H or methyl, ethyl, propyl or butyl; and

R^{21a} is, at each occurrence, independently H, methyl, ethyl, propyl or butyl, phenyl, or C_1-C_4 haloalkyl.

[10] In an even more preferred second embodiment of the present invention,

Y^1 and Y^2 are independently selected from:

a) -OH,

b) -F,

b) C_1-C_6 alkoxy, or

when taken together, Y^1 and Y^2 form:

c) a cyclic boron ester where said chain or ring contains from 2 to 12 carbon atoms, and, optionally, 1, 2, or 3 heteroatoms which can be N, S, or O,

R^1 is selected from $-CH_2CH_2CF_3$, $-CH_2CHF_2$, and $-CH_2CH_2F$,

A is A^1-A^2, A^1-A^2-A^3, or A^1-A^2-A^3-A^4;

A^1, A^2, A^3, and A^4 are independently selected from Ala, Arg, Asn, Asp, Aze, Cha, Cys, Dpa, Gln, Glu, Gly, His, Hyp, Ile, Irg, Leu, Lys, Met, Orn, Phe, Phe(4-fluoro), Pro, Sar, Ser, Thr, Trp, Tyr, Val, Asp(OMe), Glu(OMe), Hyp(OMe), Asp(O^tBu), Glu(O^tBu), Hyp(O^tBu), Thr(O^tBu), Asp(OBzl), Glu(OBzl), Hyp(OBzl), and Thr(OBzl);

R^2 is H;

R^3 is H, methyl, ethyl, propyl, butyl, phenyl, benzyl, phenylethyl-, phenylpropyl-, phenylbutyl-, $-C(=O)R^4$, $-S(=O)_2R^4$, $-C(=O)-X-(CH_2)_m-Z$, or an NH_2-blocking group;

R^4 is C_1-C_4 alkyl substituted with 0-1 R^{4A},

C_3-C_6 cycloalkyl substituted with 0-3 R^{4B} and

aryl substituted with 0-2 R^{4B} and

5-10 membered heterocyclic ring system consisting of carbon atoms and 1-4 heteroatoms selected from the group: O, S, and N, and said heterocyclic ring system is substituted with 0-2 R^{4B};

R^{4A} is C_1-C_4 alkyl, halo, $-OR^{20}$, $-SR^{20}$, $-NR^{18}R^{19}$,
phenyl substituted with 0-3 R^{4B};
naphthyl substituted with 0-3 R^{4B};
benzyl substituted with 0-3 R^{4B}; or a
5-6 membered heterocyclic ring system containing 1, 2 or 3 heteroatoms selected from nitrogen, oxygen and sulfur; said heterocyclic ring system is substituted with 0-3 R^{4B};

R^{4B} is selected at each occurrence from the group:
H, F, Cl, Br, I, $-NO_2$, $-CF_3$, $-OCF_3$, $-CH_3$, $-CH_2CH_3$, $-OCH_3$, =O, -OH, $-CO_2H$, $-SCH_3$, $-SO_3H$, $-SO_2CH_3$, $-NH_2$, $-NH(CH_3)$, $-N(CH_3)_2$, propyl, butyl, ethoxy, propoxy, butoxy, thioethoxy, thiopropoxy, thiobutoxy, cyclopropyl, cyclobutyl,
phenyl substituted with 0-3 R^{4C};
phenyl(C_1-C_4 alkyl)- substituted with 0-3 R^{4C}, and
5-6 membered heterocyclic ring system consisting of carbon atoms and 1-3 heteroatoms selected from the group: O, S, and N, and said heterocyclic ring system is substituted with 0-3 R^{4C};

R^{4C} is selected at each occurrence from the group:
H, F, Cl, Br, I, $-NO_2$, -CN, $-CF_3$, $-OCF_3$, $-CH_3$, $-OCH_3$, OH, and $-SO_2CH_3$;

X is a bond,
C_1-C_4 alkyl substituted with 0-3 R^{11},
C_2-C_4 alkenyl substituted with 0-2 R^{11},
C_3-C_{10} carbocycle substituted with 0-2 R^{11}, wherein the carbocycle is selected from cyclopropyl,

cyclobutyl, cyclopentyl, cyclohexyl, adamantanyl, norbornanyl, norbornenyl, and fluorenyl,

phenyl substituted with 0-3 R^{11},

naphthyl substituted with 0-3 R^{11},

C_5-C_{10} heterocycle substituted with 0-2 R^{11}, wherein the heterocycle is selected from furanyl, oxazolyl, isoxazolyl, benzthiophenyl, pyrrolidinyl, pyrrolyl, carbazolyl, pyridinyl, thiophenyl, triazolyl, thiadiazolyl, benzodioxanyl, benzodioxolyl, quinazolinyl, quinoxalinyl, and quinolinyl;

R^{11} at each occurrence is independently selected from H, $-CH_3$, $-CH_2CH_3$, $-NO_2$, $-NH_2$, $-SO_3H$, $-SO_2CH_3$, $-CO_2H$, $-CF_3$, $-OH$, $-OCH_3$, $-SCH_3$, $-OCF_3$, $-Cl$, $-Br$, $-I$, $-F$, $=O$, C_1-C_4 alkyl, C_1-C_4 alkoxy, C_1-C_4 thioalkoxy, phenyl, and phenyl(C_1-C_4 alkyl)-, wherein phenyl is optionally substituted with 0-3 substituents selected from $-CH_3$, $-NO_2$, $-CN$, $-OH$, $-OCH_3$, $-OCF_3$, $-SO_2CH_3$, $-CF_3$, $-Cl$, $-Br$, $-I$, and F;

alternatively, two independent R^{11} groups may optionally be taken together to form $-(CH_2)_p-$;

m is 0, 1, or 2;

p is 2, 3, or 4;

Z is selected from:

$-H$, $-R^{12}$, -halo, $-NHSO_2R^{12}$, $-SO_2NHR^{12}$, $-SO_2R^{12}$, $-C(=O)R^{12}$, $-OC(=O)C(=O)NHR^{12}$, $-NHC(=O)C(=O)OR^{12}$, $-OC(=O)R^{12}$, $-C(=O)OR^{12}$, $-OR^{12}$, $-SR^{12}$, and $-CN$;

R^{12} is H,

C_1-C_4 alkyl substituted with 0-3 R^{13},

C_3-C_{10} carbocycle substituted with 0-3 R^{13},

phenyl substituted with 0-3 R^{13}, or

C_5-C_{10} heterocycle substituted with 0-3 R^{13}; wherein the heterocycle is selected from furanyl, oxazolyl, isoxazolyl, pyrrolidinyl, pyrrolyl, pyridinyl, thiophenyl, triazolyl, and thiadiazolyl;

R^{13} at each occurrence is independently selected from H, $-CH_3$, $-CH_2CH_3$, $-NO_2$, $-SO_2OH$, $-SO_2CH_3$, $-CF_3$, -Cl, -Br, -I, -F, $-NH_2$, $-NH(CH_3)$, $-N(CH_3)_2$, $-NH(CH_2CH_3)$, $-N(CH_2CH_3)_2$, methyl, ethyl, propyl, and butyl;

R^{18} and R^{19} are independently selected from H, methyl, ethyl, propyl, butyl, benzyl, phenylethyl, cyclopropyl, cyclobutyl, cyclopentyl, and cyclohexyl; and

R^{20} is methyl, ethyl, propyl or butyl.

[11] In another even more preferred second embodiment of the present invention,

Y^1 and Y^2 are independently selected from:

a) -OH,

b) -F,

b) C_1-C_6 alkoxy, or

when taken together, Y^1 and Y^2 form:

c) a cyclic boron ester where said chain or ring contains from 2 to 12 carbon atoms, and, optionally, 1, 2, or 3 heteroatoms which can be N, S, or O,

R^1 is $-CH_2CHF_2$;

A is A^1-A^2, A^1-A^2-A^3, or A^1-A^2-A^3-A^4;

A^1, A^2, A^3, and A^4 are independently selected from Ala, Arg, Asn, Asp, Aze, Cha, Cys, Dpa, Gln, Glu, Gly, His, Hyp, Ile, Irg, Leu, Lys, Met, Orn, Phe, Phe(4-fluoro), Pro, Sar, Ser, Thr, Trp, Tyr, Val, Asp(OMe), Glu(OMe), Hyp(OMe), Asp(O^tBu), Glu(O^tBu), Hyp(O^tBu), Thr(O^tBu), Asp(OBzl), Glu(OBzl), Hyp(OBzl), and Thr(OBzl);

R^2 is H;

R^3 is H, methyl, ethyl, propyl, butyl, phenyl, benzyl, phenylethyl-, phenylpropyl-, phenylbutyl-, $-C(=O)R^4$, $-S(=O)_2R^4$, $-C(=O)-X-(CH_2)_m-Z$, or an NH_2-blocking group;

R^4 is C_1-C_4 alkyl substituted with 0-1 R^{4A},
C_3-C_6 cycloalkyl substituted with 0-3 R^{4B} and
aryl substituted with 0-2 R^{4B} and
5-10 membered heterocyclic ring system consisting of carbon atoms and 1-4 heteroatoms selected from the group: O, S, and N, and said heterocyclic ring system is substituted with 0-2 R^{4B};

R^{4A} is C_1-C_4 alkyl, halo, $-OR^{20}$, $-SR^{20}$, $-NR^{18}R^{19}$,
phenyl substituted with 0-3 R^{4B};
naphthyl substituted with 0-3 R^{4B};
benzyl substituted with 0-3 R^{4B}; or a
5-6 membered heterocyclic ring system containing 1, 2 or 3 heteroatoms selected from nitrogen, oxygen and sulfur; said heterocyclic ring system is substituted with 0-3 R^{4B};

R^{4B} is selected at each occurrence from the group:
H, F, Cl, Br, I, $-NO_2$, $-CF_3$, $-OCF_3$, $-CH_3$, $-CH_2CH_3$, $-OCH_3$, =O, -OH, $-CO_2H$, $-SCH_3$, $-SO_3H$, $-SO_2CH_3$, $-NH_2$, $-NH(CH_3)$, $-N(CH_3)_2$, propyl, butyl, ethoxy, propoxy, butoxy, thioethoxy, thiopropoxy, thiobutoxy, cyclopropyl, cyclobutyl,

phenyl substituted with 0-3 R^{4C};
phenyl(C_1-C_4 alkyl)- substituted with 0-3 R^{4C}, and
5-6 membered heterocyclic ring system consisting of carbon atoms and 1-3 heteroatoms selected from the group: O, S, and N, and said heterocyclic ring system is substituted with 0-3 R^{4C};

R^{4C} is selected at each occurrence from the group:
H, F, Cl, Br, I, $-NO_2$, -CN, $-CF_3$, $-OCF_3$, $-CH_3$, $-OCH_3$, OH, and $-SO_2CH_3$;

X is a bond,
C_1-C_4 alkyl substituted with 0-3 R^{11},
C_2-C_4 alkenyl substituted with 0-2 R^{11},
C_3-C_{10} carbocycle substituted with 0-2 R^{11}, wherein the carbocycle is selected from cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, adamantanyl, norbornanyl, norbornenyl, and fluorenyl,
phenyl substituted with 0-3 R^{11},
naphthyl substituted with 0-3 R^{11},
C_5-C_{10} heterocycle substituted with 0-2 R^{11}, wherein the heterocycle is selected from furanyl, oxazolyl, isoxazolyl, benzthiophenyl, pyrrolidinyl, pyrrolyl, carbazolyl, pyridinyl, thiophenyl, triazolyl, thiadiazolyl, benzodioxanyl, benzodioxolyl, quinazolinyl, quinoxalinyl, and quinolinyl;

R^{11} at each occurrence is independently selected from H, $-CH_3$, $-CH_2CH_3$, $-NO_2$, $-NH_2$, $-SO_3H$, $-SO_2CH_3$, $-CO_2H$, $-CF_3$, -OH, $-OCH_3$, $-SCH_3$, $-OCF_3$, -Cl, -Br, -I, -F, =O, C_1-C_4 alkyl, C_1-C_4 alkoxy, C_1-C_4 thioalkoxy, phenyl, and phenyl(C_1-C_4 alkyl)-, wherein phenyl is optionally substituted with 0-3 substituents selected from $-CH_3$, $-NO_2$, -CN, -OH, $-OCH_3$, $-OCF_3$, $-SO_2CH_3$, $-CF_3$, -Cl, -Br, -I, and F;

alternatively, two independent R^{11} groups may optionally be taken together to form $-(CH_2)_p-$;

m is 0, 1, or 2;

p is 2, 3, or 4;

Z is selected from:
-H, $-R^{12}$, -halo, $-NHSO_2R^{12}$, $-SO_2NHR^{12}$, $-SO_2R^{12}$, $-C(=O)R^{12}$, $-OC(=O)C(=O)NHR^{12}$, $-NHC(=O)C(=O)OR^{12}$, $-OC(=O)R^{12}$, $-C(=O)OR^{12}$, $-OR^{12}$, $-SR^{12}$, and -CN;

R^{12} is H,
C_1-C_4 alkyl substituted with 0-3 R^{13},
C_3-C_{10} carbocycle substituted with 0-3 R^{13},
phenyl substituted with 0-3 R^{13}, or
C_5-C_{10} heterocycle substituted with 0-3 R^{13}; wherein the heterocycle is selected from furanyl, oxazolyl, isoxazolyl, pyrrolidinyl, pyrrolyl, pyridinyl, thiophenyl, triazolyl, and thiadiazolyl;

R^{13} at each occurrence is independently selected from H, $-CH_3$, $-CH_2CH_3$, $-NO_2$, $-SO_2OH$, $-SO_2CH_3$, $-CF_3$, -Cl, -Br, -I, -F, $-NH_2$, $-NH(CH_3)$, $-N(CH_3)_2$, $-NH(CH_2CH_3)$, $-N(CH_2CH_3)_2$, methyl, ethyl, propyl, and butyl;

R^{18} and R^{19} are independently selected from H, methyl, ethyl, propyl, butyl, benzyl, phenylethyl, cyclopropyl, cyclobutyl, cyclopentyl, and cyclohexyl; and

R^{20} is methyl, ethyl, propyl or butyl.

In an even further more preferred embodiment of the present invention are compounds of Formula (I) selected from Examples 7-17, 19-22, 27-41, 43-53, 54a-54f, 59a-59bj, and 60a-60bc.

In an even further more preferred embodiment of the present invention are compounds of Formula (I) selected from Table 2.

In an even further more preferred embodiment of the present invention are compounds of Formula (I) selected from Table 3.

In an even further more preferred embodiment of the present invention are compounds of Formula (I) selected from Table 4.

In an even further more preferred embodiment of the present invention are compounds of Formula (I) selected from Table 5.

In an even further more preferred embodiment of the present invention are compounds of Formula (I) selected from Table 6.

In an even further more preferred embodiment of the present invention are compounds of Formula (I) selected from Table 7.

In a third embodiment, the present invention provides a pharmaceutical composition comprising a compound of Formula (I) and a pharmaceutically acceptable carrier.

In a fourth embodiment, the present invention provides a method for the treatment of HCV comprising administering to a host in need of such treatment a therapeutically effective amount of a compound of Formula (I), or a pharmaceutically acceptable salt thereof.

This invention also provides compositions comprising one or more of the foregoing compounds and methods of using such compositions in the treatment of hepatitis C virus, such as inhibition of hepatitis C virus protease, in mammals or as reagents used as inhibitors of hepatitis C virus protease in the processing of blood to plasma for diagnostic and other commercial purposes.

In another embodiment, the present invention provides novel compounds of Formula (I)or pharmaceutically acceptable salt forms thereof for use in therapy.

In another embodiment, the present invention provides the use of novel compounds of Formula (I) or pharmaceutically acceptable salt forms thereof for the manufacture of a medicament for the treatment of HCV.

In a most preferred embodiment of the invention substituent R^1 is $-CH_2CHF_2$.

In another most preferred embodiment of the invention substituent R^1 is $-CH_2CH_2CF_3$.

In another most preferred embodiment of the invention substituent R^1 is allyl.

As used throughout the specification, the following abbreviations for amino acid residues or amino acids apply:

Abu is L-aminobutyric acid;
Ala is L-alanine;
Alg is L-2-amino-4-pentenoic acid;
Ape is L-2-aminopentanoic acid;
Arg is L-arginine;
Asn is L-asparagine;
Asp is L-aspartic acid;

Aze is azedine-2-carboxlic acid;
Cha is L-2-amino-3-cyclohexylpropionic acid;
Cpa is L-2-amino-3-cyclopropylpropionic acid
Cpg is L-2-amino-2-cyclopropylacetic acid;
Cys is L-cysteine;
Dfb is L-4,4'-difluoro-1-amino-butyric acid;
Dpa is L-2-amino-3,3-diphenylpropionic acid
Gln is L-glutamine;
Glu is L-glutamic acid;
Gly is glycine;
His is L-histidine;
HomoLys is L-homolysine;
Hyp is L-4-hydroxyproline;
Ile is L-isoleucine;
Irg is isothiouronium analog of L-Arg;
Leu is L-leucine;
Lys is L-lysine;
Met is L-methionine;
Orn is L-ornithine;
Phe is L-phenylalanine;
Phe(4-fluoro) is para-fluorophenylalanine;
Pro is L-proline;
Sar is L-sarcosine;
Ser is L-serine;
Thr is L-threonine;
Tpa is L-2-amino-5,5,5-trifluoropentanoic acid;
Trp is L-tryptophan;
Tyr is L-tyrosine; and
Val is L-valine.

The "D" prefix for the foregoing abbreviations indicates the amino acid is in the D-configuration. "D,L" indicates the amino is present in mixture of the D- and the L-configuration. The prefix "boro" indicates amino acid residues where the carboxyl is replaced by a boronic acid or a boronic acid ester. For example, if R^1 is isopropyl and Y^1 and Y^2 are OH, the C-terminal residue is abbreviated "boroVal-OH" where "-OH" indicates the boronic acid is in

the form of the free acid. The pinanediol boronic acid ester and the pinacol boronic acid ester are abbreviated "-$C_{10}H_{16}$ " and "-C_6H_{12}", respectively. Examples of other useful diols for esterification with the boronic acids are 1,2-ethanediol, 1,3-propanediol, 1,2-propanediol, 2,3-butanediol, 1,2-diisopropylethanediol, 5,6-decanediol, and 1,2-dicyclohexylethanediol. Analogs containing sidechain substituents are described by indicating the substituent in parenthesis following the name of the parent residue. For example the analog of boroPhenylalanine containing a meta cyano group is -boroPhe(mCN)-.

The following abbreviations may also be used herein and are defined as follows. The abbreviation "DIBAL" means diisobutylaluminum hydride. The abbreviation "RaNi" means Raney nickel. The abbreviation "LAH" means lithium aluminum hydride. The abbreviation "1,1'-CDI" means 1,1'-carbonyldiimidazole. The abbreviation "Bn" means benzyl. The abbreviation "BOC" means t-butyl carbamate. The abbreviation "CBZ" means benzyl carbamate. Other abbreviations are: BSA, benzene sulfonic acid; THF, tetrahydrofuran; Boc-, t-butoxycarbonyl-; Ac-, acetyl; pNA, p-nitro-aniline; DMAP, 4-N,N-dimethylaminopyridine; Tris, Tris(hydroxymethyl)aminomethane; MS, mass spectrometry; FAB/MS, fast atom bombardment mass spectrometry. LRMS(NH_3 -CI)and HRMS(NH_3 -CI)are low and high resolution mass spectrometry, respectively, using NH_3 as an ion source.

The compounds herein described may have asymmetric centers. All chiral, diastereomeric, and racemic forms are included in the present invention. Many geometric isomers of olefins, C=N double bonds, and the like can also be present in the compounds described herein, and all such stable isomers are contemplated in the present invention. It will be appreciated that certain compounds of the present invention contain an asymmetrically substituted carbon atom, and may be isolated in optically active or

racemic forms. It is well known in the art how to prepare optically active forms, such as by resolution of racemic forms or by synthesis, from optically active starting materials. Also, it is realized that cis and trans geometric isomers of the compounds of the present invention are described and may be isolated as a mixture of isomers or as separated isomeric forms. All chiral, diastereomeric, racemic forms and all geometric isomeric forms of a structure are intended, unless the specific stereochemistry or isomer form is specifically indicated.

The reactions of the synthetic methods claimed herein are carried out in suitable solvents which may be readily selected by one of skill in the art of organic synthesis, said suitable solvents generally being any solvent which is substantially nonreactive with the starting materials (reactants), the intermediates, or products at the temperatures at which the reactions are carried out. A given reaction may be carried out in one solvent or a mixture of more than one solvent. Depending on the particular reaction step, suitable solvents for a particular reaction step may be selected.

Combinations of substituents and/or variables are permissible only if such combinations result in stable compounds. By stable compound or stable structure it is meant herein a compound that is sufficiently robust to survive isolation to a useful degree of purity from a reaction mixture, and formulation into an efficacious therapeutic agent.

The term "substituted," as used herein, means that any one or more hydrogens on the designated atom is replaced with a selection from the indicated group, provided that the designated atom's normal valency is not exceeded, and that the substitution results in a stable compound. When a substituent is keto (i.e., =O), then 2 hydrogens on the atom are replaced.

When any variable (e.g., R^{11} or R^{13}) occurs more than one time in any constituent or formula for a compound, its definition at each occurrence is independent of its definition at every other occurrence. Thus, for example, if a group is shown to be substituted with 0-2 R^{11}, then said group may optionally be substituted with up to two R^{11} groups and R^{11} at each occurrence is selected independently from the definition of R^{11}. Also, combinations of substituents and/or variables are permissible only if such combinations result in stable compounds. By stable compound it is meant herein a compound that is sufficiently robust to survive isolation to a useful degree of purity from a reaction mixture.

When a bond to a substituent is shown to cross a bond connecting two atoms in a ring, then such substituent may be bonded to any atom on the ring. When a substituent is listed without indicating the atom via which such substituent is bonded to the rest of the compound of a given formula, then such substituent may be bonded via any atom in such substituent. Combinations of substituents and/or variables are permissible only if such combinations result in stable compounds.

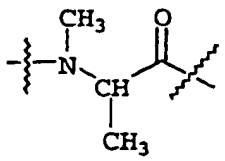
In Formula (I) the substituent A is intended to be absent (i.e. a bond), a single amino acid residue, or a peptide of 2 to 10 amino acid residues. For example, the scope of A can be described as a bond, A^1, A^1-A^2, A^1-A^2-A^3, A^1-A^2-A^3-A^4, A^1-A^2-A^3-A^4-A^5, A^1-A^2-A^3-A^4-A^5-A^6, A^1-A^2-A^3-A^4-A^5-A^6-A^7, A^1-A^2-A^3-A^4-A^5-A^6-A^7-A^8, A^1-A^2-A^3-A^4-A^5-A^6-A^7-A^8-A^9; or A^1-A^2-A^3-A^4-A^5-A^6-A^7-A^8-A^9-A^{10}. Alternatively, A can be described as $(A'')_n$ wherein n is 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10. By either description when A is comprised of two amino acid residues or greater, each amino acid residue of A is independently selected apart from each other amino acid residue. For example A^1, A^2, A^3, A^4, A^5, A^6, A^7, A^8, A^9 and A^{10}, are independently selected from the defined list of possible amino acid residues, including modified or unnatural amino acid residues, disclosed herein. Likewise,

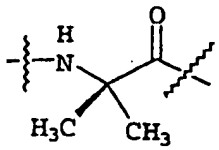
each A", when n is 2 or greater, is independently selected from the defined list of possible amino acid residues, including modified or unnatural amino acid residues, disclosed herein. Therefore, A is intended to be absent, a single amino acid residue, a homopeptide, or a heteropeptide.

A preferred scope of substituent A is A^1, A^1-A^2, A^1-A^2-A^3, A^1-A^2-A^3-A^4, A^1-A^2-A^3-A^4-A^5, and A^1-A^2-A^3-A^4-A^5-A^6. A more preferred scope of substituent A is A^1, A^1-A^2, A^1-A^2-A^3, A^1-A^2-A^3-A^4, and A^1-A^2-A^3-A^4-A^5. An even more preferred scope of substituent A is A^1-A^2, A^1-A^2-A^3, A^1-A^2-A^3-A^4, and A^1-A^2-A^3-A^4-A^5. A most preferred scope of substituent A is A^1-A^2, A^1-A^2-A^3, and A^1-A^2-A^3-A^4.

A more preferred scope of substituent A^1 is Pro, 3-hydroxyproline, 4-hydroxyproline, Hyp(OMe), Hyp(O^tBu), and Hyp(OBzl).

"Amino acid residue" as used herein, refers to natural, modified or unnatural amino acids of either D- or L-configuration and means an organic compound containing both a basic amino group and an acidic carboxyl group. Natural amino acids residues are Ala, Arg, Asn, Asp, Aze, Cys, Gln, Glu, Gly, His, Hyp, Ile, Irg Leu, Lys, Met, Orn, Phe, Phe(4-fluoro), Pro, Sar, Ser, Thr, Trp, Tyr, and Val. Roberts and Vellaccio, The Peptides, Vol 5; 341-449 (1983), Academic Press, New York, discloses numerous suitable unnatural amino acids and is incorporated herein by reference for that purpose. Additionally, said reference describes, but does not extensively list, acylic N-alkyl and acyclic α,α-disubstituted amino acids. Included in the scope of the present invention are N-alkyl, aryl, and alkylaryl analogs of both in chain and N-terminal amino acid residues. Similarly, alkyl, aryl, and alkylaryl maybe substituted for the alpha hydrogen. Illustrated below are examples of N-alkyl and alpha alkyl amino acid residues, respectively.





Modified amino acids which can be used to practice the invention include, but are not limited to, D-amino acids, hydroxylysine, 4-hydroxyproline, 3-hydroxyproline, an N-CBZ-protected amino acid, 2,4-diaminobutyric acid, homoarginine, norleucine, N-methylaminobutyric acid, naphthylalanine, phenylglycine, ß-phenylproline, tert-leucine, 4-aminocyclohexylalanine, N-methyl-norleucine, 3,4-dehydroproline, N,N-dimethylaminoglycine, N-methylaminoglycine, 4-aminopiperidine-4-carboxylic acid, 6-aminocaproic acid, trans-4-(aminomethyl)-cyclohexanecarboxylic acid, 2-, 3-, and 4-(aminomethyl)-benzoic acid, 1-aminocyclopentanecarboxylic acid, 1-aminocyclopropanecarboxylic acid, and 2-benzyl-5-aminopentanoic acid.

Unnatural amino acids that fall within the scope of this invention are by way of example and without limitation: 2-aminobutanoic acid, 2-aminopentanoic acid, 2-aminohexanoic acid, 2-aminoheptanoic acid, 2-aminooctanoic acid, 2-aminononanoic acid, 2-aminodecanoic acid, 2-aminoundecanoic acid, 2-amino-3,3-dimethylbutanoic acid, 2-amino-4,4-dimethylpentanoic acid, 2-amino-3-methylhexanoic acid, 2-amino-3-methylheptanoic acid, 2-amino-3-methyloctanoic acid, 2-amino-3-methylnonanoic acid, 2-amino-4-methylhexanoic acid, 2-amino-3-ethylpentanoic acid, 2-amino-3,4-dimethylpentanoic acid, 2-amino-3,5-dimethylhexanoic acid, 2-amino-3,3-dimethylpentanoic acid, 2-amino-3-ethyl-3-methylpentanoic acid, 2-amino-3,3-diethylpentanoic acid, 2-amino-5-methylhexanoic acid, 2-amino-6-methylheptanoic, 2-amino-7-methyloctanoic, 2-amino-2-cyclopentylacetic, 2-amino-2-cylcohexylacetic acid, 2-amino-2-(1-methylcylcohexyl)acetic acid, 2-amino-2-(2-methyl-1-methylcylcohexyl)acetic acid, 2-amino-2-(3-methyl-

1-methylcylcohexyl)acetic acid, 2-amino-2-(4-methyl-1-methylcylcohexyl)acetic acid, 2-amino-2-(1-ethylcycolhexyl)acetic acid, 2-amino-3-(cyclohexyl)propanoic acid, 2-amino-4-(cyclohexyl)butanoic acid, 2-amino-3-(1-adamantyl)propanoic acid, 2-amino-3-butenoic acid, 2-amino-3-methyl-3-butenoic acid, 2-amino-4-pentenoic acid, 2-amino-4-hexenoic acid, 2-amino-5-heptenoic acid, 2-amino-4-methyl-4-hexenoic acid, 2-amino-5-methyl-4-hexenoic acid, 2-amino-4-methy-5-hexenoic acid, 2-amino-6-heptenoic acid, 2-amino-3,3,4-trimethyl-4-pentenoic acid, 2-amino-4-chloro-4-pentenoic, 2-amino-4,4-dichloro-3-butenoic acid, 2-amino-3-(2-methylenecyclopropyl)-propanoic acid, 2-amino-2-(2-cyclopentenyl)acetic acid, 2-amino-2-(cyclohexenyl)acetic acid, 2-amino-3-(2-cyclopentenyl)propanoic acid, 2-amino-3-(3-cyclopentenyl)propanoic acid, 2-amino-3-(1-cyclohexyl)propanoic acid, 2-amino-2-(1-cyclopentenyl)acetic acid, 2-amino-2-(1-cylcohexyl)acetic acid, 2-amino-2-(1-cylcoheptenyl)acetic acid, 2-amino-2-(1-cyclooctenyl)acetic acid, 2-amino-3-(1-cycloheptenyl)propanoic acid, 2-amino-3-(1,4-cyclohexadienyl)propanoic acid, 2-amino-3-(2,5-cyclohexadienyl)propanoic acid, 2-amino-2-(7-cycloheptatrienyl)acetic acid, 2-amino-4,5-hexadienoic acid, 2-amino-3-butynoic acid, 2-amino-4-pentyoic acid, 2-amino-4-hexynoic acid, 2-amino-4-hepten-6-ynoic acid, 2-amino-3-fluoropropanoic acid, 2-amino-3,3,3-trifluoropropanoic acid, 2-amino-3-fluorobutanoic acid, 2-amino-3-fluoropentanoic acid, 2-amino-3-fluorohexanoic acid, 2-amino-3,3-difluorobutanoic acid, 2-amino-3,3-difluoro-3-phenylpropanoic acid, 2-amino-3-perfluoroethylpropanoic acid, 2-amino-3-perfluoropropylpropanoic acid, 2-amino-3-fluoro-3-methylbutanoic acid, 2-amino-5,5,5-trifluoropentanoic acid, 2-amino-3-methyl-4,4,4-trifluorobutanoic acid, 2-amino-3-trifluoromethyl-4,4,4-trifluorobutanoic acid, 2-amino-3,3,4,4,5,5-heptafluoropentanoic acid, 2-amino-3-methyl-5-fluoropentanoic acid, 2-amino-3-methyl-4-fluoropentanoic

acid, 2-amino-5,5-difluorohexanoic acid, 2-amino-4-(fluoromethyl)-5-fluoropentanoic acid, 2-amino-4-trifluoromethyl-5,5,5-trifluoropentanoic acid, 2-amino-3-fluoro-3-methylbutanoic acid, 2-amino-3-fluoro-3-phenylpentanoic acid, 2-amino-2-(1-fluorocyclopentyl)acetic acid, 2-amino-2-(1-fluorocyclohexyl)acetic acid, 2-amino-3-chloropropanoic acid acid, 2-amino-3-chlorobutanoic acid acid, 2-amino-4,4-dichlorobutanoic acid acid, 2-amino4,4,4-trichlorobutanoic acid, 2-amino-3,4,4-trichlorobutanoic acid, 2-amino-6-chlorohexanoic acid, 2-amino-4-bromobutanoic acid, 2-amino-3-bromobutanoic acid, 2-amino-3-mercaptobutanoic acid, 2-amino-4-mercaptobutanoic acid, 2-amino-3-mercapto-3,3-dimethylpropanoic acid, 2-amino-3-mercapto-3-methylpentanoic acid, 2-amino-3-mercaptopentanoic acid, 2-amino-3-mercapto-4-methylpentanoic acid, 2-amino-3-methyl-4-mercaptopentanoic acid, 2-amino-5-mercapto-5-methylhexanoic acid, 2-amino-2-(1-mercaptocyclobutyl)acetic acid, 2-amino-2-(1-mercaptocyclopentyl)acetic acid, 2-amino-2-(1-mercaptocyclohexyl)acetic acid, 2-amino-5-(methylthio)pentanoic acid, 2-amino-6-(methylthio)hexanoic acid, 2-amino-4-methylthio-3-phenylbutanoic acid, 2-amino-5-ethylthio-5-methylpentanoic acid, 2-amino-5-ethylthio-3,5,5-trimethylpentanoic acid, 2-amino-5-ethylthio-5-phenylpentanoic acid, 2-amino-5-ethylthio-5-pentanoic acid, 2-amino-5-butylthio-5-methylpentanoic acid, 2-amino-5-butylthio-3,5,5-trimethylpentanoic acid, 2-amino-5-butylthio-5-phenylpentanoic acid, 2-amino-5-(butylthio)pentanoic acid, 2-amino-3-methy4-hydroselenopentanoic acid, 2-amino-4-methylselenobutanoic acid, 2-amino-4-ethylselenobutanoic acid, 2-amino-4-benzylselenobutanoic acid, 2-amino-3-methyl-4-(methylseleno)butanoic acid, 2-amino-3-(aminomethylseleno)propanoic acid, 2-amino-3-(3-aminopropylseleno)propanoic acid, 2-amino-4-methyltellurobutanoic acid, 2-amino-4-hydroxybutanoic acid, 2-amino-4-hydroxyhexanoic acid, 2-amino-3-hydroxypentanoic acid, 2-amino-3-hydroxyhexanoic acid, 2-amino-3methyl-4-

hydroxybutanoic acid, 2-amino-3-hydroxy-3-methylbutanoic acid, 2-amino-6-hydroxyhexanoic acid, 2-amino-4-hydroxyhexanoic acid, 2-amino-3-hydroxy-4-methylpentanoic acid, 2-amino-3-hydroxy-3-methylpentanoic acid, 2-amino4-hydroxy-3,3-dimethylbutanoic acid, 2-amino-3-hydroxy4-methylpentanoic acid, 2-amino-3-hydroybutanedioic acid, 2-amino-3-hydroxy-3-phenyl-propanoic acid, 2-amino-3-hydroxy-3-(4-nitrophenyl)propanoic acid, 2-amino-3-hydroxy-3-(3-pyridyl)propanoic acid, 2-amino-2-(1-hydroxycyclopropyl)acetic acid, 2-amino-3-(1-hydroxycyclohexyl)propanoic acid, 2-amino-3-hydroxy-3-phenylpropanoic acid, 2-amino-3-hydroxy-3-[3-bis(2-chloroethyl)aminophenyl]propanoic acid, 2-amino-3-hydroxy-3-(3,4-dihydroxyphenyl)propanoic acid, 2-amino-3-hydroxy-3-(3,4-methylenedioxyphenyl)propanoic acid, 2-amino-4-fluoro-3-hydroxybutanoic acid, 2-amino-4,4,4-trichloro-3-hydroxybutanoic acid, 2-amino-3-hydroxy-4-hexynoic acid, 2-amino-3,4-dihydroxybutanoic acid, 2-amino-3,4,5,6-tetrahydroxyhexanoic acid, 2-amino-4,5-dihydroxy-3-methylpentanoic acid, 2-amino-5,6-dihydroxyhexanoic acid, 2-amino-5-hydroxy-4-(hydroxyrnethyl)pentanoic acid, 2-amino-4,5-dihydroxy-4-(hydroxymethyl)pentanoic acid, 2-amino-3-hydroxy-5-benzyloxypentanoic acid, 2-amino-3-(2-aminoethoxy)propanoic acid, 2-amino-4-(2-aminoethoxy)butanoic acid, 2-amino-4-oxobutanoic acid, 2-amino-3-oxobutanoic acid, 2-amino-4-methyl-3-oxopentanoic acid, 2-amino-3-phenyl-3-oxopropanoic acid, 2-amino-4-phenyl-3-oxobutanoic acid, 2-amino-3-methyl-4-oxopentanoic acid, 2-amino-4-oxo-4-(4-hydroxyphenyl)butanoic acid, 2-amino-4-oxo-4-(2-furyl)butanoic acid, 2-amino-4-oxo-4-(2-nitrophenyl)butanoic acid, 2-amino-4-oxo-4-(2-amino-4-chlorophenyl)butanoic acid, 2-amino-3-(4-oxo-1-cyclohexenyl)propanoic acid, 2-amino-3-(4-oxocyclohexanyl)propanoic acid, 2-amino-3-(2,5-dimethyl-3,6-dioxo-1,4-cydohexadienyl)propanoic acid, 2-amino-3-(1-hydroxy-5-methyl-7-oxo-cyclohepta-1,3,5-trien-2-yl)propanoic acid, 2-amino-3-(1-hydroxy-7-oxo-cyclohepta-1,3,5-trien-3-yl)propanoic acid, 2-amino-3-(1-hydroxy-7-

oxo-cyclohepta-1,3,5-trien-4-yl)propanoic acid, 2-amino-4-methoxy-3-butenoic acid, 2-amino-4-(2-aminoethoxy)-3-butenoic acid, 2-amino-4-(2-amino-3-hydroxypropyl)-3-butenoic acid, 2-amino-2-(4-methoxy-1,4-cyclohexadienyl)acetic acid, 2-amino-3,3-diethoxypropanoic acid, 2-amino-4,4-dimethylbutanoic acid, 2-amino-2-(2,3-epoxycyclohexyl)acetic acid, 2-amino-3-(2,3-epoxycyclohexy)propanoic acid, 2-amino-8-oxo-9,10-epoxydecanoic acid, 2-amino-propanedioic acid, 2-amino-3-methylbutanedioic acid, 2-amino-3,3-dimethylbutanedioic acid, 2-amino4-methylpentanedioic acid, 2-amino-3-methylpentanedioic acid, 2-amino-3-phenylpentanedioic acid, 2-amino-3-hydroxypentanedioic acid, 2-amino-3-carboxypentanedioic acid, 2-amino-4-ethylpentanedioic acid, 2-amino-4-propylpentanedioic acid, 2-amino-4-isoamylpentanedioic acid, 2-amino-4-phenylpentanedioic acid, 2-amino-hexanedioic acid, 2-amino-heptanedioic acid, 2-amino-decanedioic acid, 2-amino-octanedioic acid, 2-amino-dodecanedioic acid, 2-amino-3-methylenebutanedioic acid, 2-amino-4-methylenepentanedioic acid, 2-amino-3-fluorobutanedioic acid, 2-amino-4-fluoropentanedioic acid, 2-amino-3,3-difluorobutanedioic acid, 2-amino-3-chloropentanedioic acid, 2-amino-3-hydroxybutanedioic acid, 2-amino-4-hydroxypentanedioic acid, 2-amino-4-hydroxyhexanedioic acid, 2-amino-3,4-dihydroxypentanedioic acid, 2-amino-3-(3-hydroxypropyl)butanedioic acid, 2-amino-3-(1-carboxy-4-hydroxy-2-cyclodienyl)propanoic acid, 2-amino-3-(aceto)butanedioic acid, 2-amino-3-cyanobutanedioic acid, 2-amino-3-(2-carboxy-6-oxo-6H-pyranyl)propanoic acid, 2-amino-3-carboxybutanedioic acid, 2-amino-4-carboxypentanedioic acid, 3-amido-2-amino-3-hydroxypropanoic acid, 3-arnido-2-amino-3-methylpropanoic acid, 3-amido-2-amino-3-phenylpropanoic acid, 3-amido-2,3-diaminopropanoic acid, 3-amido-2-amino-3-[N-(4-hydroxyphenyl)amino]propanoic acid, 2,3-diaminopropanoic acid, 2,3-diaminobutanoic acid, 2,4-diaminobutanoic acid) 2,4-diamino-3-methylbutanoic acid, 2,4-diamino-3-phenylbutanoic acid, 2-amino-3-(methylamino)butanoic acid,

2,5-diamino-3-methylpentanoic acid, 2,7-diaminoheptanoic acid, 2,4-diaminoheptanoic acid, 2-amino-2-(2-piperidyl)acetic acid, 2-amino-2-(1-aminocyclohexyl)acetic acid, 2,3-diamino-3-phenylpropanoic acid, 2,3-diamino-3-(4-hydroxyphenyl)propanoic acid, 2,3-diamino-3-(4-methoxyphenyl)propanoic acid, 2,3-diamino-3-[4-(N,N'-dimethyamino)phenyl]propanoic acid, 2,3-diamino-3-(3,4-dimethoxyphenyl)propanoic acid, 2,3-diamino-3-(3,4-methylenedioxyphenyl)propanoic acid, 2,3-diamino-3-(4-hydroxy-3-methoxyphenyl)propanoic acid, 2,3-diamino-3-(2-phenylethyl)propanoic acid, 2,3-diamino-3-propylpropanoic acid, 2,6-diamino-4-hexenoic acid, 2,5-diamino-4-fluoropentanoic acid, 2,6-diamino-5-fluorohexanoic acid, 2,6-diamino-4-hexynoic acid, 2,6-diamino-5,5-difluorohexanoic acid, 2,6-diamino-5,5-dimethylhexanoic acid, 2,5-diamino-3-hydroxypentanoic acid, 2,6-diamino-3-hydroxyhexanoic acid, 2,5-diamino-4-hydroxypentanoic acid, 2,6-diamino-4-hydroxyhexanoic acid, 2,6-diamino-4-oxohexanoic acid, 2,7-diaminooctanedioic acid, 2,6-diamino-3-carboxyhexanoic acid, 2,5-diamino-4-carboxypentanoic acid, 2-amino-4-(2-(N,N'-diethylamino)ethyl)pentandioic acid, 2-amino-4-(N,N'-diethylamino)pentandioic acid, 2-amino-4-(N-morpholino)pentandioic acid, 2-amino-4-(N,N'-bis(2-chloroethyl)amino)pentandioic acid, 2-amino-4-(N,N'-bis(2-hydroxyethyl)amino)pentandioic acid, 2,3,5-triaminopentanoic acid, 2-amino-3-(N-(2-aminethyl)amino)propanoic acid, 2-amino-3-((2-aminoethyl)seleno)propanoic acid, 2-amino-3-[(2-aminoethyl)thio]propanoic acid, 2-amino4-aminooxybutanoic acid, 2-amino-5-hydroxyaminopentanoic acid, 2-amino-5-[N-(5-nitro-2-pyrimidinyl)amino]pentanoic acid, 2-amino-4-[(7-nitro-2,1,3-benzoxadiazol-4-yl)amino]butanoic acid, 2-amino-3-guanidinopropanoic acid, 2-amino-3-guanidinobutanoic acid, 2-amino-4-guanidobutanoic acid, 2-amino-6-guanidohexanoic acid, 2-amino-6-ureidohexanoic acid, 2-amino-3-(2-iminoimidiazolin-4-yl)propanoic acid, 2-amino-2-(2-iminohexahydropyrimidin-4-yl)acetic acid, 2-amino-3-(2-iminohexahydropyrimidiny-4-yl)propanoic acid, 2-

amino4-fluoro-5-guanidopentanoic acid, 2-amino-4-hydroxy-5-guanidopentanoic acid, 2-amino-4-guanidooxybutanoic acid, 2-amino-6-amidinohexanoic acid, 2-amino-5-(N-acetimidoylamino)pentanoic acid, 1-aminocyclopropanecarboxylic acid, 1-amino4-ethylcyclpropanecarboxylic acid, 1-aminocyclopentanecarboxylic acid, 1-aminocyclopentanecarboxylic acid, 1-amino-2,2,5,5-tetramethyl-cyclohexanecarboxylic acid, 1-aminocydoheptanecarboxylic acid, 1-aminocyclononanecarboxylic acid, 2-aminoindan-2-carboxylic acid, 2-aminonorbornane-2-carboxylic acid, 2-amino-3-phenylnorbornane-2-carboxylic acid, 3-aminotetrahydrothiophene-3-carboxylic acid, 1-amino-1,3-cyclohexanedicarboxylic acid, 3-aminopyrrolidine-3-carboxylic acid, 1,4-diaminocyclohexanecarboxylic acid, 6-alkoxy-3-amino-1,2,3,4-tetrahydrocarbazole-3-carboxylic acid, 2- aminobenzobicyclo[2,2,2]octane-2-carboxylic acid, 2-aminoindan-2-carboxylic acid, 1-amino-2-(3,4-dhydroxyphenyl)cyclopropanecarboxylic acid, 5,6-dialkoxy-2-aminoindane-2-carboxylic acid, 4,5-dihydroxy-2-aminoindan-2-caroxylic acid, 5,6-dihydroxy-2-aminotetralin-2-carboxylic acid, 2-amino-2-cyanoacetic acid, 2-amino-3-cyanopropanoic acid, 2-amino-4-cyanobutanoic acid, 2-amino-5-nitropentanoic acid, 2-amino-6-nitrohexanoic acid, 2-amino-4-aminooxybutanoic acid, 2-amino-3-(N-nitrosohydroxyamino)propanoic acid, 2-amino-3-ureidopropanoic acid, 2-amino-4-ureidobutanoic acid, 2-amino-3-phosphopropanoic acid, 2-amino-3-thiophosphopropanoic acid, 2-amino-4-methanephosphonylbutanoic acid, 2-amino-3-(trimethylsilyl)propanoic acid, 2-amino-3-(dimethyl(trimethylsilylmethylsilyl)propanoic acid, 2-amino-2-phenylacetic acid, 2-amino-2-(3-chlorophenyl)acetic acid, 2-amino-2-(4-chlorophenyl)acetic acid, 2-amino-2-(3-fluorophenyl)acetic acid, 2-amino-2-(3-methylphenyl)acetic acid, 2-amino-2-(4ofluorophenyl)acetic acid, 2-amino-2-(4-methylphenyl)acetic acid, 2-amino-2-(4-methoxyphenyl)acetic

acid, 2-amino-2-(2-fluorophenyl)acetic acid, 2-amino-2-(2-methylphenyl)acetic acid, 2-amino-2-(4-chloromethylphenyl)acetic acid, 2-amino-2-(4-hydroxymethylphenyl)acetic acid, 2-amino-2-[4-(methylthiomethyl)phenyl]acetic acid, 2-amino-2-(4-bromomethylphenyl)acetic acid, 2-amino-2-(4-(methoxymethy)phenyl)acetic acid, 2-amino-2-(4-((N-benzylamino)methyl)phenyl)acetic acid, 2-amino-2-(4-hydroxylphenyl)acetic acid, 2-amino-2-(3-hydroxylphenyl)acetic acid, 2-amino-2-(3-carboxyphenyl)acetic acid, 2-amino-2-(4-aminophenyl)acetic acid, 2-amino-2-(4-azidophenyl)acetic acid, 2-amino-2-(3-t-butyl-4-hydroxyphenyl)acetic acid, 2-amino-2-(3,5-difluoro-4-hydroxyphenyl)acetic acid, 2-amino-2-(3,5-dihydroxyphenyl)acetic acid, 2-amino-2-(3-carboxy-4-hydroxyphenyl)acetic acid, 2-amino-2-(3,5-di-t-butyl-4-hydroxyphenyl)acetic acid, 2-amino-3-(2-methylphenyl)propanoic acid, 2-amino-3-(4-ethylphenyl)propanoic acid, 2-amino-3-(4-phenylphenyl)propanoic acid, 2-amino-3-(4-benzylphenyl)propanoic acid, 2-amino-3-(3-fluorophenyl)propanoic acid, 2-amino-3-(4-methylphenyl)propanoic acid, 2-amino-3-(4-fluorophenyl)propanoic acid, 2-amino-3-(4-chlorophenyl)propanoic acid, 2-amino-3-(2-chlorophenyl)propanoic acid, 2-amino-3-(4-bromophenyl)propanoic acid, 2-amino-3-(2-bromophenyl)propanoic acid, 2-amino-3-(3-hydroxyphenyl)propanoic acid, 2-amino-3-(2-hydroxyphenyl)propanoic acid, 2-amino-3-(4-mercaptophenyl)propanoic acid, 2-amino-3-(3-trifluoromethylphenyl)propanoic acid, 2-amino-3-(3-hydroxyphenyl)propanoic acid, 2-amino-3-(4-hydroxyphenyl)propanoic acid, 2-amino-3-[4-(hydroxymethy)phenyl]propanoic acid, 2-amino-3-[3-(hydroxymethyl)phenyl]propanoic acid, 2-amino-3-[3-(aminomethyl)phenyl]propanoic acid, 2-amino-3-(3-carboxyphenyl)propanoic acid, 2-amino-3-(4-

nitrophenyl)propanoic acid, 2-amino-3-(4-aminophenyl)propanoic acid, 2-amino-3-(4-azidophenyl)propanoic acid, 2-amino-3-(4-cyanophenyl)propanoic acid, 2-amino-3-(4-acetophenyl)propanoic acid, 2-amino-3-(4-guanidinophenyl)propanoic acid, 2-amino-3-[4-(phenylazo)phenyl]propanoic acid, 2-amino-3-[4-(2-phenylethylenyl)phenyl]propanoic acid, 2-amino-3-(4-trialkylsilylphenyl)propanoic acid, 2-amino-3-(2,4-dimethylphenyl)propanoic acid, 2-amino-3-(2,3-dimethylphenyl)propanoic acid, 2-amino-3-(2,5-dimethylphenyl)propanoic acid, 2-amino-3-(3,5-dimethylphenyl)propanoic acid, 2-amino-3-(2,4,6-trimethylphenyl)propanoic acid, 2-amino-3-(3,4,5-trimethylphenyl)propanoic acid, 2-amino-3-(2,3,4,5,6-pentamethylphenyl)propanoic acid, 2-amino-3-(2,4,-difluorophenyl)propanoic acid, 2-amino-3-(3,4,-difluorophenyl)propanoic acid, 2-amino-3-(2,5,-difluorophenyl)propanoic acid, 2-amino-3-(2,6,-difluorophenyl)propanoic acid, 2-amino-3-(2,3,5,6-tetrafluorophenyl)propanoic acid, 2-amino-3-(3,5-dichloro-2,4,6-trifluorophenyl)propanoic acid, 2-amino-3-(2,3-difluorophenyl)propanoic acid, 2-amino-3-(2,3-bistrifluoromethylphenyl)propanoic acid, 2-amino-3-(2,4-bistrifluoromethylphenyl)propanoic acid, 2-amino-3-(2-chloro-5-trifluoromethylphenyl)propanoic acid, 2-amino-3-(2,5-difluorophenyl)propanoic acid, 2-amino-3-(2,3,4,5,6-pentafluorophenyl)propanoic acid, 2-amino-3-(2,3-dibromophenyl)propanoic acid, 2-amino-3-(2,5-dibromophenyl)propanoic acid, 2-amino-3-(3,4-dibromophenyl)propanoic acid, 2-amino-3-(3,4,5-triiodophenyl)propanoic acid, 2-amino-3-(2,3-dihydroxyphenyl)propanoic acid, 2-amino-3-(2,5-dihydroxyphenyl)propanoic acid, 2-amino-3-(2,6-dihydroxyphenyl)propanoic acid, 2-amino-3-(3-bromo-5-methoxyphenyl)propanoic acid, 2-amino-3-(2,5-dimethoxyphenyl)propanoic acid, 2-amino-3-(2,5-dimethoxy-4-methylphenyl)propanoic acid, 2-amino-3-(4-bromo-2,5-

dimethoxyphenyl)propanoic acid, 2-amino-3-(3-carboxy-4-hydroxyphenyl)propanoic acid, 2-amino-3-(3-carboxy-4-aminophenyl)propanoic acid, 2-amino-3-(2-hydroxy-5-nitrophenyl)propanoic acid, 2-amino-3-(2-ethoxy-5-nitrophenyl)propanoic acid, 2-amino-3-(3,4,5-trimethoxyphenyl)propanoic acid, 2-amino-3-(4-azido-2-nitrophenyl)propanoic acid, 2-amino-3-(2-hydroxy-5-nitrophenyl)propanoic acid, 2-amino-3-(2,4-bis-trimethylsilylphenyl)propanoic acid, 2-amino-3-(4-hydroxy-3,5-di-t-butylphenyl)propanoic acid, 2-amino-3-(4-hydroxy-3-benzylphenyl)propanoic acid, 2-amino-3-(4-hydroxy-3-fluorophenyl)propanoic acid, 2-amino-3-(4-hydroxy-2,3,5,6-tetrafluorophenyl)propanoic acid, 2-amino-3-(4-hydroxy-3,5-dichlorophenyl)propanoic acid, 2-amino-3-(4-hydroxy-3-iodophenyl)propanoic acid, 2-amino-3-(4-hydroxy-3,5-diiodophenyl)propanoic acid, 2-amino-3-(4-hydroxy-2-hydroxyphenyl)propanoic acid, 2-amino-3-(4-hydroxy-3-hydroxymethylphenyl)propanoic acid, 2-amino-3-(4-hydroxy-2-hydroxy-6-methylphenyl)propanoic acid, 2-amino-3-(4-hydroxy-3-carboxyphenyl)propanoic acid, 2-amino-3-(4-hydroxy-3,5-dinitrophenyl)propanoic acid, substituted thyronines, 2-amino-3-(3,4-dihydroxy-2-chlorophenyl)propanoic acid, 2-amino-3-(3,4-dihydroxy-2-bromophenyl)propanoic acid, 2-amino-3-(3,4-dihydroxy-2-fluorophenyl)propanoic acid, 2-amino-3-(3,4-dihydroxy-2-nitrophenyl)propanoic acid, 2-amino-3-(3,4-dihydroxy-2-methylphenyl)propanoic acid, 2-amino-3-(3,4-dihydroxy-2-ethylphenyl)propanoic acid, 2-amino-3-(3,4-dihydroxy-2-isopropylphenyl)propanoic acid, 2-amino-3-(2-t-butyl-4,5-dihydroxyphenyl)propanoic acid, 2-amino-3-(3-fluoro-4,5-dihydroxyphenyl)propanoic acid, 2-amino-3-(2-fluoro-4,5-dihydroxyphenyl)propanoic acid, 2-amino-3-(2,5,6-trifluoro-3,4-dihydroxyphenyl)propanolc acid, 2-amino-3-(2,6-dibromo-3,4-dihydroxyphenyl)propanoic acid, 2-amino-3-(5,6-dibromo-3,4-dihydroxyphenyl)propanoic acid, 2-amino-3-(2,4,5-trihydroxyphenyl)propanoic acid, 2-amino-3-(2,3,4-trihydroxyphenyl)propanoic acid, 2-amino-3-(3,4-dihydroxy-5-methoxyphenyl)propanoic acid, 2-amino-3-methyl-3-

phenylpropanoic acid, 2-amino-3-ethyl-3-phenylpropanoic acid, 2-amino-3-isopropyl-3-phenylpropanoic acid, 2-amino-3-butyl-3-phenylpropanoic acid, 2-amino-3-benzyl-3-phenylpropanoic acid, 2-amino-3-phenylethyl-3-phenylpropanoic acid, 2-amino-3-(4-chlorophenyl)-3-phenylpropanoic acid, 2-amino-3-(4-methoxyphenyl)-3-phenylpropanoic acid, 2-amino-3,3-diphenylpropanoic acid, 2-amino-3-[4-(N,N- diethylamino)phenyl]heptanoic acid, 2-amino-3-[4-(N,N-diethylamino)phenyl]pentanoic acid, 2-amino-3-(3,4-dimethoxyphenyl)pentanoic acid, 2-amino-3-(3,4-dihydroxyphenyl)pentanoic acid, 2-amino-3-methyl-3-phenylbutanoic acid, 2-amino-3-ethyl-3-phenylpentanoic acid, 2-amino-3-methyl-3-phenylpentanoic acid, 2-amino-3,3-diphenylbutanoic acid, 2-amino-3-fluoro-3-phenylpropanoic acid, 2-amino-3-methylene-3-phenylpropanoic acid, 2-amino-3-methylmercapto-3-phenylpropanoic acid, 2-amino-4-methylmercapto-4-phenylbutanoic acid, 2-amino-4-(3,4-dihydroxyphenyl)butanoic acid, 2-amino-5-(4-methoxyphenyl)pentanoic acid, 2-amino-4-phenylbutanoic acid, 2-amino-5-phenylpentanoic acid, 2-amino-3,3-dimethyl-5-phenylpentanoic acid, 2-amino-4-phenyl-3-butenoic acid, 2-amino-4-phenoxybutanoic acid, 2-amino-5-phenoxypentanoic acid, 2-amino-2-(indanyl)acetic acid, 2-amino-2-(1-tetralyl)acetic acid, 2-amino-4,4-diphenylbutanoic acid, 2-amino-2-(2-naphthyl)acetic acid, 2-amino-3-(1-naphthyl)propanoic acid, 2-amino-3-(1-naphthyl)pentanoic acid, 2-amino-3-(2-naphthyl)propanoic acid, 2-amino-3-(1-chloro-2-naphthyl)propanoic acid, 2-amino-3-(1-bromo-2-naphthyDpropanoic acid, 2-amino-3-(4-hydroxy-1-naphthyl)propanoic acid, 2-amino-3-(4-methoxy-1-naphthyl)propanoic acid, 2-amino-3-(4-hydroxy-2-chloro-1-naphthyl)propanoic acid, 2-amino-3-(2-chloro-4-methoxy-1-naphthyl)propanoic acid, 2-amino-2-(2-anthryl)acetic acid, 2-amino-3-(9-anthryl)propanoic acid, 2-amino-3-(2-fluorenyl)propanoic acid, 2-amino-3-(4-fluorenyl)propanoic acid, 2-amino-3-(carboranyl)propanoic acid, 3-methylproline, 4-methylproline, 5-methylproline, 4,4-dimethylproline, 4-fluoroproline, 4,4-difluoroproline, 4-

bromoproline, 4-chloroproline, 3,4-dehydroproline, 4-methylproline, 4-methyleneproline, 4-mercaptoproline, 4-(4-methoxybenzylmercapto)proline, 4-hydroxymethylproline, 3-hydroxyproline, 3-hydroxy-5-methylproline, 3,4-dihydroxyproline, 3-phenoxyproline, 3-carbamylalkylproline, 4-cyano-5-methyl-5-carboxyproline, 4,5-dicarboxyl-5-methylproline, 2-aziridinecarboxylic acid, 2-azetidinecarboxylic acid, 4-methyl-2-azetidinecarboxylic acid, pipecolic acid, 1,2,3,6-tetrahydropicolinic acid, 3,4-methyleneproline, 2.4-methyleneproline, 4-aminopipecolic acid, 5-hydroxypipecolic acid, 4,5-dihydroxypipecolic acid, 5,6-dihydroxy-2,3-dihydroindole-2-carboxylic acid, 1,2,3,4-tetrahydroquinoline-2-carboxylic acid, 6,7-dihydroxy-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid, 6-hydroxy-1-methyl-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid, 6,7-dihydroxy-1-methyl-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid, 1,3-oxazolidine-4-carboxylic acid, 1,2-oxazolidine-3-carboxylic acid, perhydro-1,4-thiazine-3-carboxylic acid, 2,2-dimethylthiazolidine-4-carboxylic acid, perhydro-1,3-thlazine-2-carboxylic acid, selenazolidine4-carboxylic acid, 2-phenylthiazolidine4-carboxylic acid, 2-(4-carboxylicyl)thiazolidine-4-carboxylic acid, 1,2,3,4,4a,9a-hexahydro-beta-carboline-3-carboxylic acid, 2,3,3a,8a-tetrahydropyrrolo(2,3b)indole-2-carboxylic acid, 2-amino-3-(2-pyridyl)propanoic acid, 2-amino-3-(3-pyridyl)propanoic acid, 2-amino-3-(4-pyridyl)propanoic acid, 2-amino-3-(2-bromo-3-pyridyl)propanoic acid, 2-amino-3-(2-bromo-4-pyridyl)propanoic acid, 2-amino-3-(2-bromo-5-pyridyl)propanoic acid, 2-amino-3-(2-bromo-6-pyridyl)propanoic acid, 2-amino-3-(2-chloro-3-pyridyl)propanoic acid, 2-amino-3-(2-chloro-4-pyridyl)propanoic acid, 2-amino-3-(2-chloro-5-pyridyl)propanoic acid, 2-amino-3-(2-chloro-6-pyridyl)propanoic acid, 2-amino-3-(2-fluoro-3-pyridyl)propanoic acid, 2-amino-3-(2-fluoro-4-pyridyl)loropanoic acid, 2-amino-3-(2-fluoro-5-pyridyl)propanoic acid, 2-amino-3-(2-fluoro-6-

pyridyl)proloanoic acid, 2-amino-3-(1,2-dihydro-2-oxo-3-pyridyl)propanoic acid, 2-amino-3-(1,2-dihydro-2-oxo4-pyridyl)propanoic acid, 2-amino-3-(1,2-dihydro-2-oxo-5-pyridyl)propanoic acid, 2-amino-3-(1,2-dihydro-2-oxo-6-pyridyl)propanoic acid, 2-amino-3-(5-hydroxy-2-pyridyl)propanoic acid, 2-amino-3-(5-hydroxy-6-iodo-2-pyridyl)propanoic acid, 2-amino-3-(3-hydroxy-4-oxo-1,4dihydro-1-pyridyl)propanoic acid, N-(5-caroxyl-5-aminopentyl)pyridinium chloride, 1,2,5-trimethyl-4-(2-amino-2-carboxy-1-hydroxyethyl)pyridinium chloride, 2-amino-2-(5-chloro-2-pyridyl)acetic acid, N-(3-amino-3-carboxypropyl)pyridinium chloride, 2-amino-3-(2-pyrryl)propanoic acid, 2-amino-3-(1-pyrryl)propanoic acid, 2-amino-4-(1-pyrryl)butanoic acid, 2-amino-5-(1-pyrryl)pentanoic acid, 2-amino-3-(5-imidazolyl)-3-methylpropanoic acid, 2-amino-3-(5-imidazolyl)-3-ethylpropanoic acid, 2-amino-3-hexyl-3-(5-imidazolyl)propanoic acid, 2-amino-3-hydroxy-3-(5-imidazolyl)propanoic acid, 2-amino-3-(4-nitro-5-imidazolyl)proloanoic acid, 2-amino-3-(4-methyl-5-imidazolyl)propanoic acid, 2-amino-3-(2-methyl-5-imidazolyl)propanoic acid, 2-amino-3-(4-fluoro-5-imidazolyl)propanoic acid, 2-amino-3-(2-fluoro-5-imidazolyl)propanoic acid, 2-amino-3-(2-amino-5-imidazolyl)propanoic acid, 2-amino-3-(2-phenylaza-5-imidazolyl)propanoic acid, 2-amino-3-(1-methyl-2-nitro-5-imidazolyl)propanoic acid, 2-amino-3-(1-methyl4-nitro-5-imidazolyl)propanoic acid, 2-amino-3-(1-methyl-5-nitro-5-imidazolyl)propanoic acid, 2-amino-3-(2-mercapto-5-imidazolyl)propanoic acid, 2-amino-4-(5-imidazolyl)butanoic acid, 2-amino-3-(1-imidazolyl)propanoic acid, 2-amino-3-(2-imidazolyl)propanoic acid, 2-amino-(1-pyrazolyl)propanoic acid, 2-amino-(3-pyrazolyl)propanoic acid, 2-amino-(3,5-dialkyl-4-pyrazolyl)propanoic acid, 2-amino-3-(3-amino-1,2,4-triazol-1-yl)propanoic acid, 2-amino-3-(tetrazol-5-yl)propanoic acid, 2-amino-4-(5-tetrazolyl)butanoic acid, 2-amino-3-(6-methyl-3-indolyl)propanoic acid, 2-amino-3-(4-fluoro-3-indolyl)propanoic acid, 2-amino-3-(5-fluoro-3-

indolyl)propanoic acid, 2-amino-3-(6-fluoro-3-indolyl)propanoic acid, 2-amino-3-(4,5,6,7-tetrafluoro-3-indolyl)propanoic acid, 2-amino-3-(5-chloro-3-indolyl)propanoic acid, 2-amino-3-(6-chloro-3-indolyl)propanoic acid, 2-amino-3-(7-chloro-3-indolyl)propanoic acid, 2-amino-3-(5-bromo-3-indolyl)propanoic acid, 2-amino-3-(7-bromo-3-indolyl)propanoic acid, 2-amino-3-(2-hydroxy-3-indolyl)propanoic acid, 2-amino-3-(5-hydroxy-3-indolyl)propanoic acid, 2-amino-3-(7-hydroxy-3-indolyl)propanoic acid, 2-amino-3-(2-alkylmercapto-3-indolyl)propanoic acid, 2-amino-3-(7-amino-3-indolyl)propanoic acid, 2-amino-3-(4-nitro-3-indolyl)propanoic acid, 2-amino-3-(7-nitro-3-indolyl)propanoic acid, 2-amino-3-(4-carboxy-3-indolyl)propanoic acid, 2-amino-3-(3-indolyl)butanoic acid, 2-amino-3-(2,3-dihydro-3-indolyl)propanoic acid, 2-amino-3-(2,3-dihydro-2-oxo-3-indolyl)propanoic acid, 2-amino-3-alkylmercapto-3-(3-indolyl)propanoic acid, 2-amino-3-(4-aza-3-indolyl)propanoic acid, 2-amino-3-(7-aza-3-indolyl)propanoic acid, 2-amino-3-(7-aza-6-chloro-4-methyl-3-indolyl)propanoic acid, 2-amino-3-(2,3-dihydrobenzofuran-3-yl)propanoic acid, 2-amino-3-(3-methyl-5-7-dialkylbenzofuran-2-yl)propanoic acid, 2-amino-3-(benzothiophen-3-yl)propanoic acid, 2-amino-3-(5-hydroxybenzothiophen-3-yl)propanoic acid, 2-amino-3-eoenzoselenol-3yl)propanoic acid, 2-amino-3-quinolylpropanoic acid, 2-amino-3-(8-hydroxy-5-quinolyl)propanoic acid, 2-amino-2-(5,6,7,8-tetrahydroquinol-5-yl)acetic acid, 2-amino-3-(3-coumarinyl)propanoic acid, 2-amino-2-(benzisoxazol-3-yl)acetic acid, 2-amino-2-(5-methylbenzisoxazol-3-yl)acetic acid, 2-amino-2-(6-methylbenzisoxazol-3-yl)acetic acid, 2-amino-2-(7-methylbenzisoxazol-3-yl)acetic acid, 2-amino-2-(5-bromobenzisoxazol-3-yl)acetic acid, 2-amino-3-(benzimidazol-2-yl)propanoic acid, 2-amino-3-(5,6-dichlorobenzimidazol-2-yl)propanoic acid, 2-amino-3-(5,6-dimethylbenzimidazol-2-yl)propanoic acid, 2-amino-3-

(4,5,6,7-hydrobenzirnidazol-2-yl)propanoic acid, 2-amino-2-(benzimidazol-5-yl)acetic acid, 2-amino-2-(1,3-dihydro-2,2-dioxoisobenzothiophen-5-yl)acetic acid, 2-amino-2-(1,3-dihydro-2,2-dioxo-2,1,3-benzothiadiazol-5-yl)acetic acid, 2-amino-2-(2-oxobenzimidazol-5-yl)acetic acid, 2-amino-3-(4-hydroxybenzothiazol-6-yl)propanoic acid, 2-amino-3-(benzoxazol-2-yl)propanoic acid, 2-amino-3-(benzothiazol-2-yl)propanoic acid, 2-amino-3-(9-adeninyl)propanoic acid, 2-amino-2-(6-chloro-9-purinyl)acetic acid, 2-amino-2-(6-amino-9-purinyl)acetic acid, 2-amino-3-(6-purinyl)propanoic acid, 2-amino-3-(8-theobrominyl)propanoic acid, 2-amino-2-(1-uracilyl)acetic acid, 2-amino-2-(1-cytosinyl)acetic acid, 2-amino-3-(1-uracilyl)propanoic acid, 2-amino-3-(1-cytosinyl)propanoic acid, 2-amino-4-(1-pyrimidinyl)butanoic acid, 2-amino-4-(4-amino-1-pyrimidinyl)butanoic acid, 2-amino-4-(4-hydroxy-1-pyrimidinyl)butanoic acid, 2-amino-5-(1-pyrimidinyl)pentanoic acid, 2-amino-5-(4-amino-1-pyrimidinyl)pentanoic acid, 2-amino-5-(4-hydroxy-1-pyrimidinyl)pentanoic acid, 2-amino-3-(5-pyrimidinyl)propanoic acid, 2-amino-3-(6-uracilyl)propanoic acid, 2-amino-3-(2-pyrimidinyl)propanoic acid, 2-amino-3-(6-amino-4-chloro-2-pyrimidinyl)propanoic acid, 2-amino-3-(4-hydroxy-2-pyrimidinyl)propanoic acid, 2-amino-3-(2-amino-4-pyrimidinyl)propanoic acid, 2-amino-3-(4,5-dihydroxypyrimidin-2-yl)propanoic acid, 2-amino-3-(2-thiouracil-6-yl)propanoic acid, 2-amino-2-(5-alkyl-2-tetrahydrofuryl)acetic acid, 2-amino-2-(5-methyl-2,5-dihydro-2-furyl)acetic acid, 2-amino-2-(5-alkyl-2-furyl)acetic acid, 2-amino-2-(2-furyl)acetic acid, 2-amino-2-(3-hydroxy-5-methyl-4-isoxazolyl)acetic acid, 2-amino-3-(4-bromo-3-hydroxy-5-isoxazolyl)propanoic acid, 2-amino-3-(4-methyl-3-hydroxy-5-isoxazolyl)propanoic acid, 2-amino-3-(3-hydroxy-5-isoxazolyl)propanoic acid, 2-amino-2-(3-chloro-D2 -isoxazolin-5-yl)acetic acid, 2-amino-2-(3-oxo-5-isoxazolidinyl)acetic acid, 2-amino-3-(3,5-dioxo-1,2,4-oxadiazolin-2-yl)propanoic acid, 2-amino-3-(3-phenyl-5-isoxazolyl)propanoic acid, 2-amino-3-[3-(4-hydroxyphenyl)-1,2,4-oxadiazol-5-yl]propanoic acid, 2-amino-3-(2-

thienyl)propanoic acid, 2-amino-2-(2-furyl)acetic acid, 2-amino-2-(2-thienyl)acetic acid, 2-amino-2-(2-thiazolyl)acetic acid, 2-amino-3-(2-thiazolyl)propanoic acid, 2-amino-4-(4-carboxy-2-thiazolyl)butanoic acid, 2-amino-3-(4-thiazolyl)propanoic acid, 2-amino-3-(2-selenolyl)propanoic acid, 2-amino-3-(2-amino-4-selenolyl)propanoic acid, and 2-amino-3-(beta-ribofuranosyl)propanoic acid.

"Amino acids residue" also refers to various amino acids where sidechain functional groups are modified with appropriate protecting groups known to those skilled in the art. "The Peptides", Vol 3, 3-88 (1981)discloses numerous suitable protecting groups and is incorporated herein by reference for that purpose. Examples of amino acids where sidechain functional groups are modified with appropriate protecting groups include, but are not limited to, Asp(OMe), Glu(OMe), Hyp(OMe), Asp(O^tBu), Glu(O^tBu), Hyp(O^tBu), Thr(O^tBu), Asp(OBzl), Glu(OBzl), Hyp(OBzl), and Thr(OBzl); wherein OMe is methoxy, O^tBu is tert-butoxy, and OBzl is benzyloxy.

As used herein, "alkyl" or "alkylene" is intended to include both branched and straight-chain saturated aliphatic hydrocarbon groups having the specified number of carbon atoms; for example, "C_1-C_6 alkyl" denotes alkyl having 1 to 6 carbon atoms. Examples of alkyl include, but are not limited to, methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, sec-butyl, t-butyl, n-pentyl, n-hexyl, 2-methylbutyl, 2-methylpentyl, 2-ethylbutyl, 3-methylpentyl, and 4-methylpentyl.

"Alkenyl" or "alkenylene" is intended to include hydrocarbon chains of either a straight or branched configuration having the specified number of carbon atoms and one or more unsaturated carbon-carbon bonds which may occur in any stable point along the chain. Examples of alkenyl include, but are not limited to, ethenyl, 1-propenyl, 2-propenyl, 2-butenyl, 3-butenyl, 2-pentenyl, 3, pentenyl, 4-pentenyl, 2-hexenyl, 3-hexenyl, 4-hexenyl, 5-

hexenyl, 2-methyl-2-propenyl, 4-methyl-3-pentenyl, and the like.

"Alkynyl" or "alkynylene" is intended to include hydrocarbon chains of either a straight or branched configuration and one or more carbon-carbon triple bonds which may occur in any stable point along the chain, such as ethynyl, propynyl, butynyl, pentynyl, hexynyl and the like.

"Cycloalkyl" is intended to include saturated ring groups, having the specified number of carbon atoms. For example, "C_3-C_6 cycloalkyl" denotes such as cyclopropyl, cyclobutyl, cyclopentyl, or cyclohexyl.

"Alkoxy" or "alkyloxy" represents an alkyl group as defined above with the indicated number of carbon atoms attached through an oxygen bridge. Examples of alkoxy include, but are not limited to, methoxy, ethoxy, n-propoxy, i-propoxy, n-butoxy, s-butoxy, t-butoxy, n-pentoxy, and s-pentoxy. Similarly, "alkylthio" or "thioalkoxy" represents an alkyl group as defined above with the indicated number of carbon atoms attached through a sulpher bridge.

"Halo" or "halogen" as used herein refers to fluoro, chloro, bromo, and iodo; and "counterion" is used to represent a small, negatively charged species such as chloride, bromide, hydroxide, acetate, sulfate, and the like.

"Haloalkyl" is intended to include both branched and straight-chain saturated aliphatic hydrocarbon groups having the specified number of carbon atoms, substituted with 1 or more halogen (for example $-C_vF_w$ where v = 1 to 3 and w = 1 to (2v+1)). Examples of haloalkyl include, but are not limited to, trifluoromethyl, trichloromethyl, pentafluoroethyl, pentachloroethyl, 2,2,2-trifluoroethyl, heptafluoropropyl, and heptachloropropyl. Examples of haloalkyl also include "fluoroalkyl" which is intended to include both branched and straight-chain saturated aliphatic hydrocarbon groups having the specified number of carbon atoms, substituted with 1 or more fluorine atoms.

As used herein, "carbocycle" is intended to mean any stable 3- to 7-membered monocyclic or bicyclic or 7- to 13-membered bicyclic or tricyclic, any of which may be saturated, partially unsaturated, or aromatic. Examples of such carbocycles include, but are not limited to, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, adamantyl, cyclooctyl, [3.3.0]bicyclooctane, [4.3.0]bicyclononane, [4.4.0]bicyclodecane (decalin), [2.2.2]bicyclooctane, fluorenyl, phenyl, naphthyl, indanyl, adamantyl, or tetrahydronaphthyl (tetralin).

As used herein, the term "heterocycle" or "heterocyclic ring" is intended to mean a stable 5- to 7-membered monocyclic or bicyclic or 7- to 14-membered bicyclic heterocyclic ring which is saturated partially unsaturated or unsaturated (aromatic), and which consists of carbon atoms and 1, 2, 3 or 4 heteroatoms independently selected from the group consisting of N, O and S and including any bicyclic group in which any of the above-defined heterocyclic rings is fused to a benzene ring. The nitrogen and sulfur heteroatoms may optionally be oxidized. The heterocyclic ring may be attached to its pendant group at any heteroatom or carbon atom which results in a stable structure. The heterocyclic rings described herein may be substituted on carbon or on a nitrogen atom if the resulting compound is stable. If specifically noted, a nitrogen in the heterocycle may optionally be quaternized. It is preferred that when the total number of S and O atoms in the heterocycle exceeds 1, then these heteroatoms are not adjacent to one another. It is preferred that the total number of S and O atoms in the heterocycle is not more than 1.

Examples of heterocycles include, but are not limited to, 1H-indazole, 2-pyrrolidonyl, 2H,6H-1,5,2-dithiazinyl, 2H-pyrrolyl, 3H-indolyl, 4-piperidonyl, 4aH-carbazole, 4H-quinolizinyl, 6H-1,2,5-thiadiazinyl, acridinyl, azocinyl, benzimidazolyl, benzofuranyl, benzothiofuranyl, benzothiophenyl, benzoxazolyl, benzoxazolinyl, benzthiazolyl, benztriazolyl, benztetrazolyl,

benzisoxazolyl, benzisothiazolyl, benzimidazalonyl, carbazolyl, 4a*H*-carbazolyl, b-carbolinyl, chromanyl, chromenyl, cinnolinyl, decahydroquinolinyl, 2*H*,6*H*-1,5,2-dithiazinyl, dihydrofuro[2,3-*b*]tetrahydrofuran, furanyl, furazanyl, imidazolidinyl, imidazolinyl, imidazolyl, imidazolopyridinyl, 1*H*-indazolyl, indolenyl, indolinyl, indolizinyl, indolyl, isatinoyl, isobenzofuranyl, isochromanyl, isoindazolyl, isoindolinyl, isoindolyl, isoquinolinyl, isothiazolyl, isothiazolopyridinyl, isoxazolyl, isoxazolopyridinyl, morpholinyl, naphthyridinyl, octahydroisoquinolinyl, oxadiazolyl, 1,2,3-oxadiazolyl, 1,2,4-oxadiazolyl, 1,2,5-oxadiazolyl, 1,3,4-oxadiazolyl, oxazolidinyl, oxazolyl, oxazolopyridinyl, oxazolidinylperimidinyl, oxindolyl, phenanthridinyl, phenanthrolinyl, phenarsazinyl, phenazinyl, phenothiazinyl, phenoxathiinyl, phenoxazinyl, phthalazinyl, piperazinyl, piperidinyl, pteridinyl, piperidonyl, 4-piperidonyl, pteridinyl, purinyl, pyranyl, pyrazinyl, pyrazolidinyl, pyrazolinyl, pyrazolopyridinyl, pyrazolyl, pyridazinyl, pyridooxazole, pyridoimidazole, pyridothiazole, pyridinyl, pyridyl, pyrimidinyl, pyrrolidinyl, pyrrolinyl, pyrrolyl, quinazolinyl, quinolinyl, 4*H*-quinolizinyl, quinoxalinyl, quinuclidinyl, carbolinyl, tetrahydrofuranyl, tetrahydroisoquinolinyl, tetrahydroquinolinyl, 6*H*-1,2,5-thiadiazinyl, 1,2,3-thiadiazolyl, 1,2,4-thiadiazolyl, 1,2,5-thiadiazolyl, 1,3,4-thiadiazolyl, thianthrenyl, thiazolyl, thiazolopyridinyl, thienyl, thienothiazolyl, thienooxazolyl, thienoimidazolyl, thiophenyl, triazinyl, 1,2,3-triazolyl, 1,2,4-triazolyl, 1,2,5-triazolyl, 1,3,4-triazolyl, and xanthenyl. Preferred heterocycles include, but are not limited to, pyridinyl, furanyl, thienyl, pyrrolyl, pyrazolyl, pyrazinyl, piperazinyl, imidazolyl, indolyl, benzimidazolyl, 1*H*-indazolyl, oxazolidinyl, benzotriazolyl, benzisoxazolyl, benzoxazolyl, oxindolyl, benzoxazolinyl, benzthiazolyl, benzisothiazolyl, isatinoyl, isoxazolopyridinyl, isothiazolopyridinyl, thiazolopyridinyl, oxazolopyridinyl, imidazolopyridinyl,

and pyrazolopyridinyl. Preferred 5 to 6 membered heterocycles include, but are not limited to, pyridinyl, furanyl, thienyl, pyrrolyl, pyrazolyl, pyrazinyl, piperazinyl, imidazolyl, and oxazolidinyl. Also included are fused ring and spiro compounds containing, for example, the above heterocycles.

As used herein, the term "aryl", or aromatic residue, is intended to mean an aromatic moiety containing the specified number of carbon atoms, such as phenyl, pyridinyl and naphthyl.

"NH_2-blocking group" as used herein, refers to various acyl, thioacyl, alkyl, sulfonyl, phosphoryl, and phosphinyl groups comprised of 1 to 20 carbon atoms. Substitutes on these groups maybe either alkyl, aryl, alkylaryl which may contain the heteroatoms, O, S, and N as a substituent or in-chain component. A number of NH_2-blocking groups are recognized by those skilled in the art of organic synthesis. By definition, an NH_2-blocking group may be removable or may remain permanently bound to the NH_2. Examples of suitable groups include formyl, acetyl, benzoyl, trifluoroacetyl, and methoxysuccinyl; aromatic urethane protecting groups, such as, benzyloxycarbonyl; and aliphatic urethane protecting groups, such as t-butoxycarbonyl or adamantyloxycarbonyl. Gross and Meinhoffer, eds., The Peptides, Vol 3; 3-88 (1981), Academic Press, New York, and Greene and Wuts Protective Groups in Organic Synthesis, 315-405 (1991), J. Wiley and Sons, Inc., New York disclose numerous suitable amine protecting groups and they are incorporated herein by reference for that purpose. Amine protecting groups may include, but are not limited to the following: 2,7-di-t-butyl-[9-(10,10-dioxo-10,10,10,10-tetrahydrothio-xanthyl)]methylo xycarbonyl; 2-trimethylsilylethyloxycarbonyl; 2-phenylethyloxycarbonyl; 1,1-dimethyl-2,2-dibromoethyloxycarbonyl; 1-methyl-1-(4-biphenylyl)ethyloxycarbonyl; benzyloxycarbonyl; p-nitrobenzyloxycarbonyl; 2-(p-

toluenesulfonyl)ethyloxycarbonyl; m-chloro-p-acyloxybenzyloxycarbonyl; 5-benzyisoxazolylmethyloxycarbonyl; p-(dihydroxyboryl)benzyloxycarbonyl; m-nitrophenyloxycarbonyl; o-nitrobenzyloxycarbonyl; 3,5-dimethoxybenzyloxycarbonyl; 3,4-dimethoxy-6-nitrobenzyloxycarbonyl; N'-p-toluenesulfonylaminocarbonyl; t-amyloxycarbonyl; p-decyloxybenzyloxycarbonyl; diisopropylmethyloxycarbonyl; 2,2-dimethoxycarbonylvinyloxycarbonyl; di(2-pyridyl)methyloxycarbonyl; 2-furanylmethyloxycarbonyl; phthalimide; dithiasuccinimide; 2,5-dimethylpyrrole; benzyl; 5-dibenzylsuberyl; triphenylmethyl; benzylidene; diphenylmethylene; or methanesulfonamide.

The phrase "pharmaceutically acceptable" is employed herein to refer to those compounds, materials, compositions, and/or dosage forms which are, within the scope of sound medical judgment, suitable for use in contact with the tissues of human beings and animals without excessive toxicity, irritation, allergic response, or other problem or complication, commensurate with a reasonable benefit/risk ratio.

As used herein, "pharmaceutically acceptable salts" refer to derivatives of the disclosed compounds wherein the parent compound is modified by making acid or base salts thereof. Examples of pharmaceutically acceptable salts include, but are not limited to, mineral or organic acid salts of basic residues such as amines; alkali or organic salts of acidic residues such as carboxylic acids; and the like. The pharmaceutically acceptable salts include the conventional non-toxic salts or the quaternary ammonium salts of the parent compound formed, for example, from non-toxic inorganic or organic acids. For example, such conventional non-toxic salts include those derived from inorganic acids such as hydrochloric, hydrobromic, sulfuric, sulfamic, phosphoric, nitric and the like; and the salts prepared from organic acids such as acetic,

propionic, succinic, glycolic, stearic, lactic, malic, tartaric, citric, ascorbic, pamoic, maleic, hydroxymaleic, phenylacetic, glutamic, benzoic, salicylic, sulfanilic, 2-acetoxybenzoic, fumaric, toluenesulfonic, methanesulfonic, ethane disulfonic, oxalic, isethionic, and the like.

The pharmaceutically acceptable salts of the present invention can be synthesized from the parent compound which contains a basic or acidic moiety by conventional chemical methods. Generally, such salts can be prepared by reacting the free acid or base forms of these compounds with a stoichiometric amount of the appropriate base or acid in water or in an organic solvent, or in a mixture of the two; generally, nonaqueous media like ether, ethyl acetate, ethanol, isopropanol, or acetonitrile are preferred. Lists of suitable salts are found in *Remington's Pharmaceutical Sciences*, 17th ed., Mack Publishing Company, Easton, PA, 1985, p. 1418, the disclosure of which is hereby incorporated by reference.

"Prodrugs" are intended to include any covalently bonded carriers which release the active parent drug according to formula (I) *in vivo* when such prodrug is administered to a mammalian subject. Prodrugs of a compound of formula (I) are prepared by modifying functional groups present in the compound in such a way that the modifications are cleaved, either in routine manipulation or *in vivo*, to the parent compound. Prodrugs include compounds of formula (I) wherein a hydroxy, amino, or sulfhydryl group is bonded to any group that, when the prodrug or compound of formula (I) is administered to a mammalian subject, cleaves to form a free hydroxyl, free amino, or free sulfhydryl group, respectively. Examples of prodrugs include, but are not limited to, acetate, formate and benzoate derivatives of alcohol and amine functional groups in the compounds of Formula (I), and the like.

"Stable compound" and "stable structure" are meant to indicate a compound that is sufficiently robust to survive isolation to a useful degree of purity from a reaction

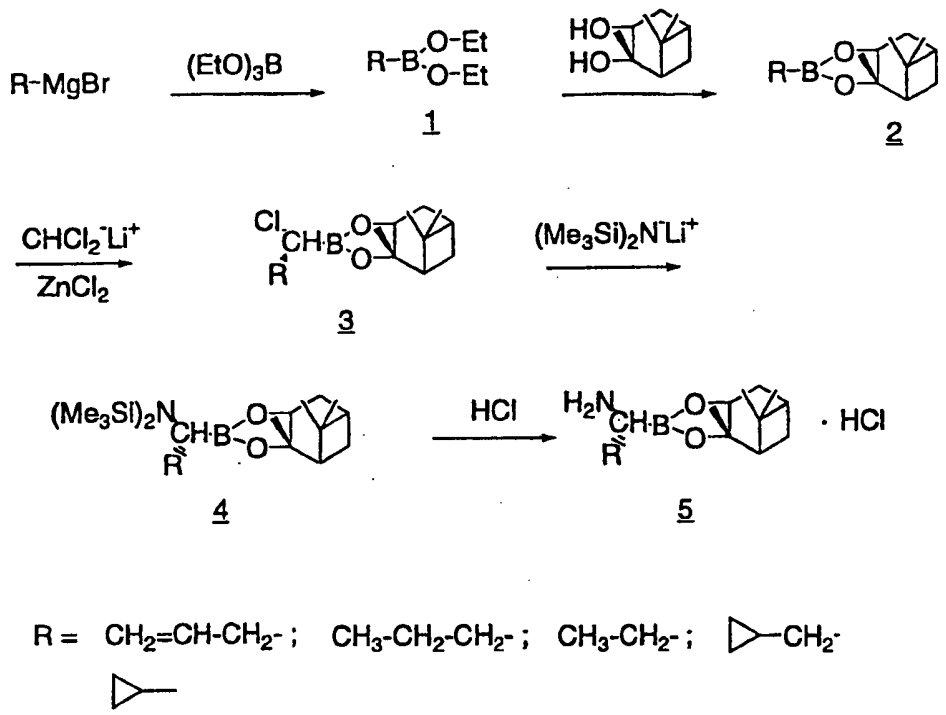
mixture, and formulation into an efficacious therapeutic agent.

SYNTHESIS

Preparation of Inhibitors

Scheme 1 shows the synthesis of α-aminoboronic acids containing sidechains where R is ethyl, allyl, vinyl, and cyclopropyl. A Grignard reagent is added to a trialkyl boronate to give a substituted dialkyl boronate. Transesterification with a suitable diol protecting group gives the boronate ester **2**. **2** is shown protected as the pinanediol ester. This is the preferred protecting group, but *C2* symmetrical diol such as (*R,R*)2,3-butandiol, and (*R,R*)dicyclohexaneethanediol can also be used effectively as well as pinacol. Other diol protecting groups are known to those skilled in the art. The α-chloroalkyl intermediate **3** is obtained by the addition of the anion of methylene chloride to the boronic acid ester. $Li^+CHCl_2^-$ is prepared in situ by the addition of LDA to a -78°C solution of the alkyl boronic acid ester in methylene chloride. Alternately, $CHCl_2^-Li^+$ is prepared by reacting *n*-butyl lithium with methylene chloride at -100°C followed by the addition of the alkyl boronic acid **2**. $ZnCl_2$ is added to more hindered alkyl boronic acid. **3** is treated with the lithium salt of hexamethyldisilazane to give the *bis*-silane protected amine **4**. Compound **4** is treated with either anhydrous HCl or trifluoroacetic acid to give the amine **5** as a hydrochloride salt or trifluoroacetate salt.

Scheme 1



R = CH_2=CH-CH_2- ; CH_3-CH_2-CH_2- ; CH_3-CH_2- ; ;

Scheme 2a outlines a novel method of preparing α-aminoboronic acids suitable for incorporation in to peptide and applied as enzyme inhibitors. Previously, Matteson (Matteson and Majumdar *J. Organometallic Chem.* 170, 259-264, 1979; Matteson and Arne *Organometallics* 1, 280-288, 1982) prepared α-haloboronic acids by this method, but did not expand this method to the preparation of α-aminoboronic acids with primary or secondary amino groups required for the preparation of peptides. Compound 6 is prepared by the method described by Sadhu and Matteson *Organometallics* 4, 1687-1689, 1985. Compound 6 is allowed to react with thiophenol in presence of tertiary base to give the thiol ether 7. Alternately, 7 can be prepared by reacting the lithium salt of thioanisole with a trialkyl boronate as described by Matteson and Arne *Organometallics* 1, 280-288 (1982). 7 is treated with LDA followed by a hydrocarbon containing an electrophilic center. For this reaction 1-bromo-2,2-difluoroethane was used to give an a 2,2-difluoroethyl substituent 8. The α-aminoboronic acid 9 was

obtained by treating 8 with methyl iodide or other suitable alkylating agent in the presence of iodide ion followed by lithium hexamethyldisilazane and HCl. In contrast to other procedures for preparing α-aminoboronic acids where the sidechain is introduced as a nucleophile or an alkene, the sidechain substituent is an electrophile. This provides a method of preparing 2-amino-3,3-difluoropropyl boronic acid where conventional methods have failed. For example, hydroboration of 1,1'-difluoroethene to give difluoroethyl boronate failed. It was our expectation that 1,1'-difluoroethyl boronate could be treated with $CHCl_2^-Li^+$ in a manner analogous to 3 in Scheme 1. In another approach, reaction of CHF_2-CH_2Br with *t*-butyllithium in a metallation reaction and treatment with triisopropyl bornate to give an intermediate similar to 2 in Scheme 1 failed. Treatment of CHF_2-CH_2Br with Mg metal and adding the resulting solution to dichlorometyl boronate also failed. Treatment of an aldehyde with DAST (Middleton *J. Org. Chem.* 40, 574-578, 1975) provides another method of introducing the $-CHF_2$ group. Attempts to prepared the corresponding protected aldehyde in a manner analogous to that described by Mantri et al. *J. Org. Chem.* 61 5690-5692 (1996) was not possible due to reagent instability.

The chemistry outlined in Scheme 2a is readily applied to the synthesis of additional compounds. 7 is allowed to react with *t*-butyl bromoacetate to yield an intermediate with a carboxylmethyl sidechain. Completion of the series of reactions in Scheme 2a gives H-boroAsp(O^tBu)-$C_{10}H_{16}$•HCl. This compound is readily incorporated into a peptide and the sidechain protecting group is removed with anhydrous HCl to give peptide-boroAsp-$C_{10}H_{16}$. Similarly, H-boroAsp(OMe)- $C_{10}H_{16}$ can be synthesized from methyl bromoacetate and the final product is obtained by treating the sidechain methyl ester with potassium trimethylsilanolate (Laganis and Chenard *Tetrahedron Letters* 25, 5831-5834, 1984).

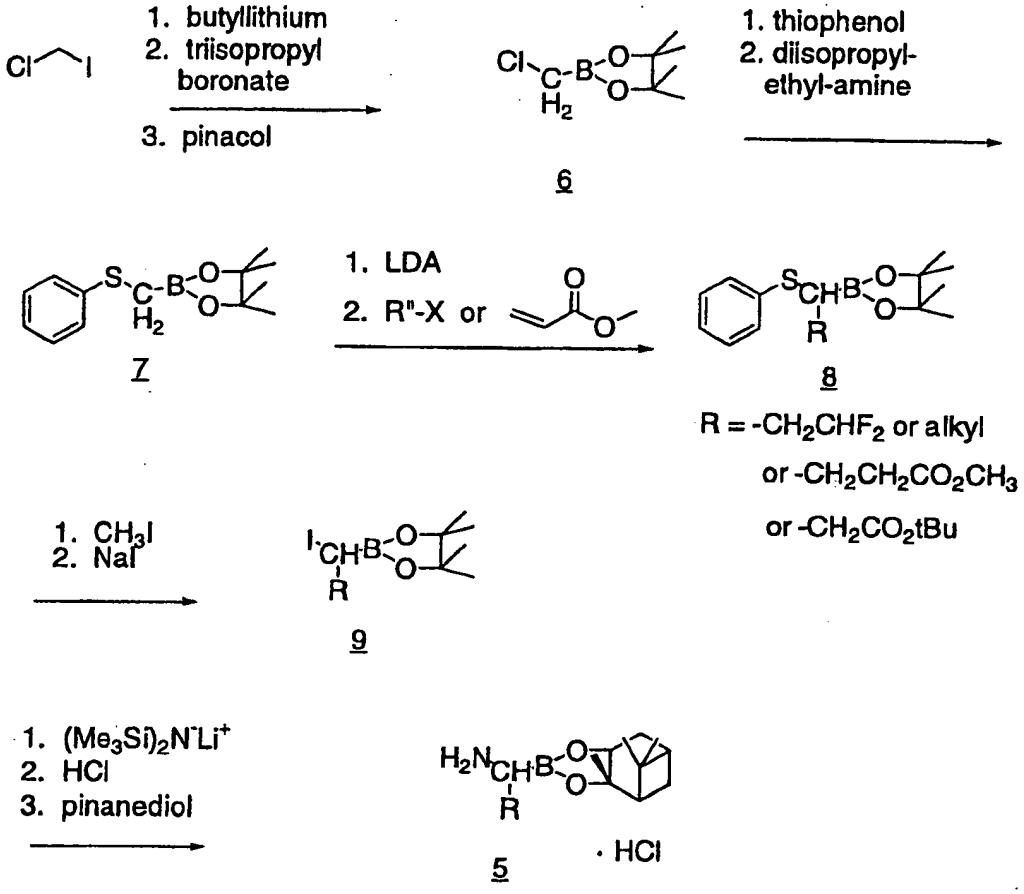
H-boroGlu-$C_{10}H_{16}$ is also readily prepared by the sequence of reactions shown in Scheme 2a. After treatment of 7 with base to generate the anion at the α-position, a Michael acceptor (in this case methyl acrylate) is added to give 8 where R= $-CH_2-CH_2-C(O)OMe$. This precursor is converted to H-boroGlu(OMe)-$C_{10}H_{16}$ which is readily incorporated into peptides. The sidechain methyl ester is cleaved with potassium trimethylsilanolate. Both boroAsp-$C_{10}H_{16}$ and boroGlu-$C_{10}H_{16}$ peptides can be converted to the corresponding boroAsn-$C_{10}H_{16}$ and -boroGln-$C_{10}H_{16}$ by coupling the sidechain carboxylate with ammonia.

α-Aminoacids containing a sidechain carboxylate (either as an ester or free carboxylate) are novel. Attempts to make boronic acid analog of aspartic acid and glutamic acid following the reaction scheme shown in Scheme 1 have failed. In Scheme 1, compounds containing a carboxylate, R= $-CH_2-C(O)O^tBu$ or $-CH_2-CH_2-C(O)-O^tBu$, failed to react to give 3. Apparently, the methylene adjacent to the carboxylate is of sufficient acidity that it reacts with $CHCl_2^-Li^+$ required for the generation of 3. Note that $^tBuO-C(O)-CH_2-CH_2-CHCl-BO_2C_{10}H_{16}$ is disclosed in the literature, but additional chemistry to convert this compound to H-boroGlu(O^tBu)-$C_{10}H_{16}$ was not done (Matteson and Beedle, *Tetrahedron Letters* 28, 4499-4502, 1987). Regardless, analytical data was not provided for the literature compound or subsequent derivatives. We were unable to prepare the α-chloro-compound following the published procedure.

In the preparation of H-boroGlu(O^tBu)-$C_{10}H_{16}$, 8 was not obtained when the anion of 7 was allowed to react with *t*-butyl 3-bromopropionate due to the acidity of the methylene α to the carboxylate. However, the anion of 7 readily adds to Michael acceptors (in this case methyl acrylate). The sequence of reactions shown in Scheme 2a has made it possible to prepare much more structurally diverse α-

aminoboronic acids. In addition to the specific compounds we have prepared, higher order acrylates or alkyl halides can be used to give more complex sidechains. This is particularly valuable for the preparation of compounds with sidechains containing sensitive groups such as ketones, phosphonates and sulfonamides.

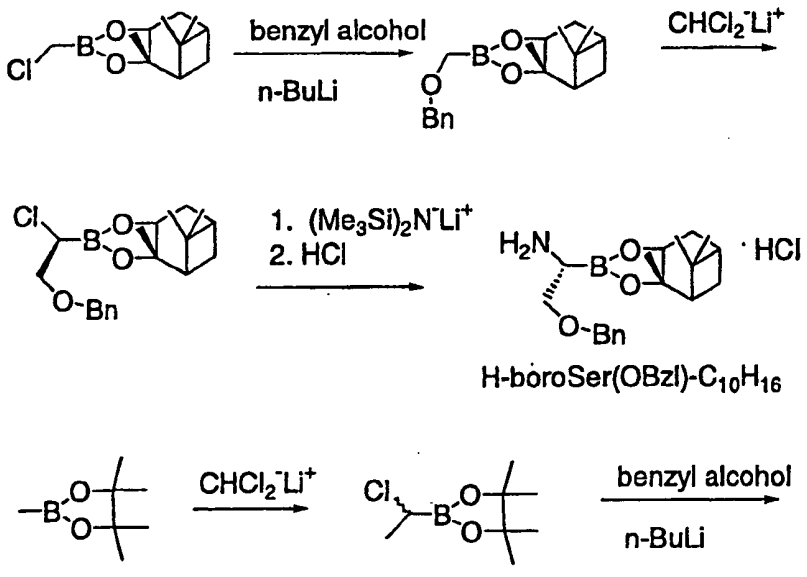
Scheme 2a

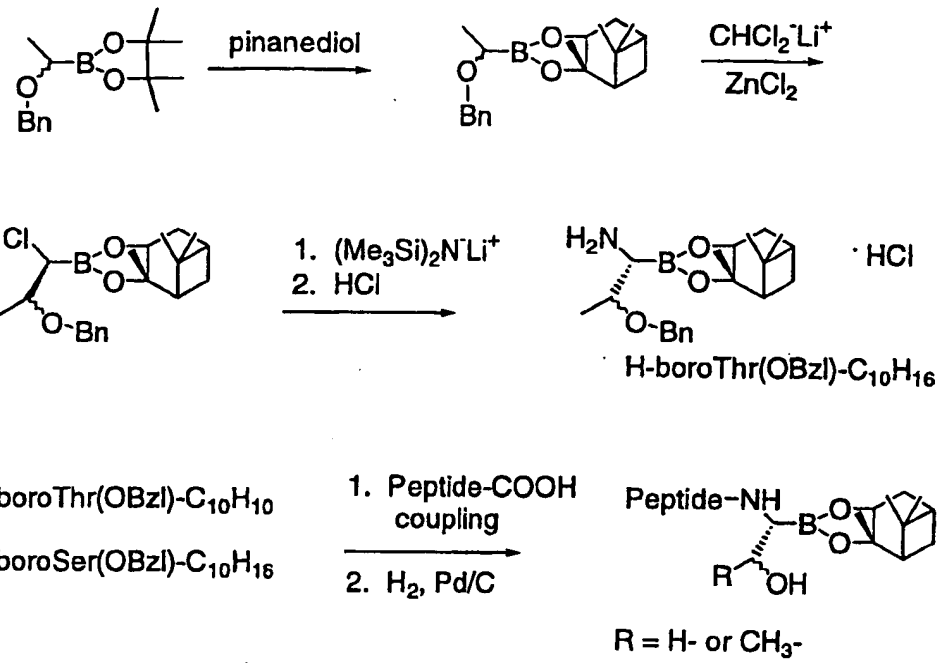


Scheme 2b illustrates the preparation of α-aminoboronic acids with hydroxy substituted side chains, boroSerine and boroThreonine. Both are synthesized as their benzyl protected form and incorporated into peptides. The benzyl protecting groups are removed by catalytic hydrogenation to give the final product. The synthesis of

2-benzyloxy-1-chloroethane boronic acids esters has been described previously (Matteson et al. *Organometallics* 3, 1284-1288, 1984), but this chemistry has not been extended to the preparation of α-aminoboronic acids. For H-boroSer(OBzl)-$C_{10}H_{16}$, the α-chloromethyl boronic acid is treated with the anion of benzyl alcohol to give the benzyl ether. Homologation with the anion of methylene chloride gives the α-chloro compound. It is readily converted to the α-aminoboronic acid by conventional procedures. Borothreonine is prepared by a similar procedure except an α-chloroethyl boronic acid ester is prepared and converted to the benzyl protected alcohol. Homologation with $CHCl_2^-Li^+$ and treatment with $(Me_3Si)_2N^-Li^+$ and HCl gives H-boroThr(OBzl)-$C_{10}H_{16}$. The first series of reactions were conducted using the pinacol ester which resulted the nonstereo specific introduction of the O-benzyl hydroxy group. This group can be introduced in the natural configuration *R*-configuation by using (*S,S*)dicyclohexaneethanediol as a chiral directing boronic acid protecting group.

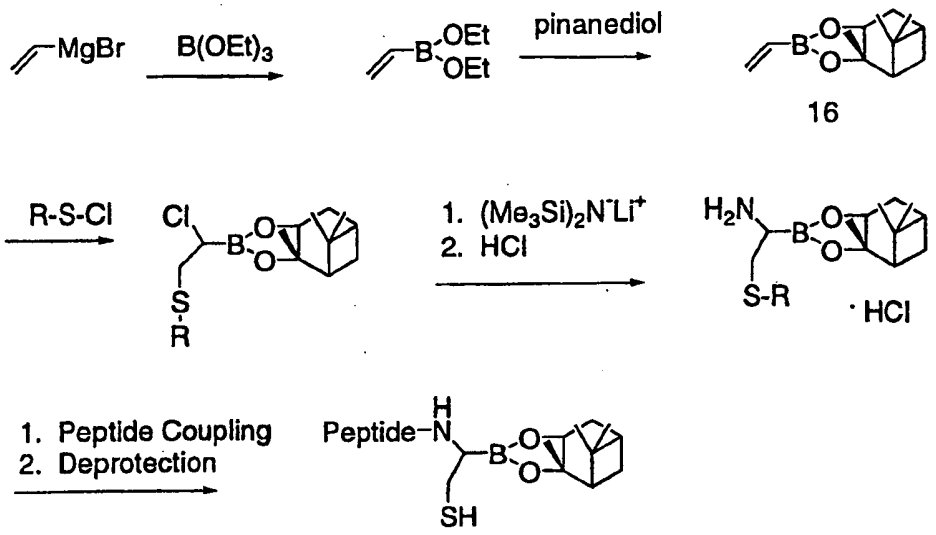
Scheme 2b





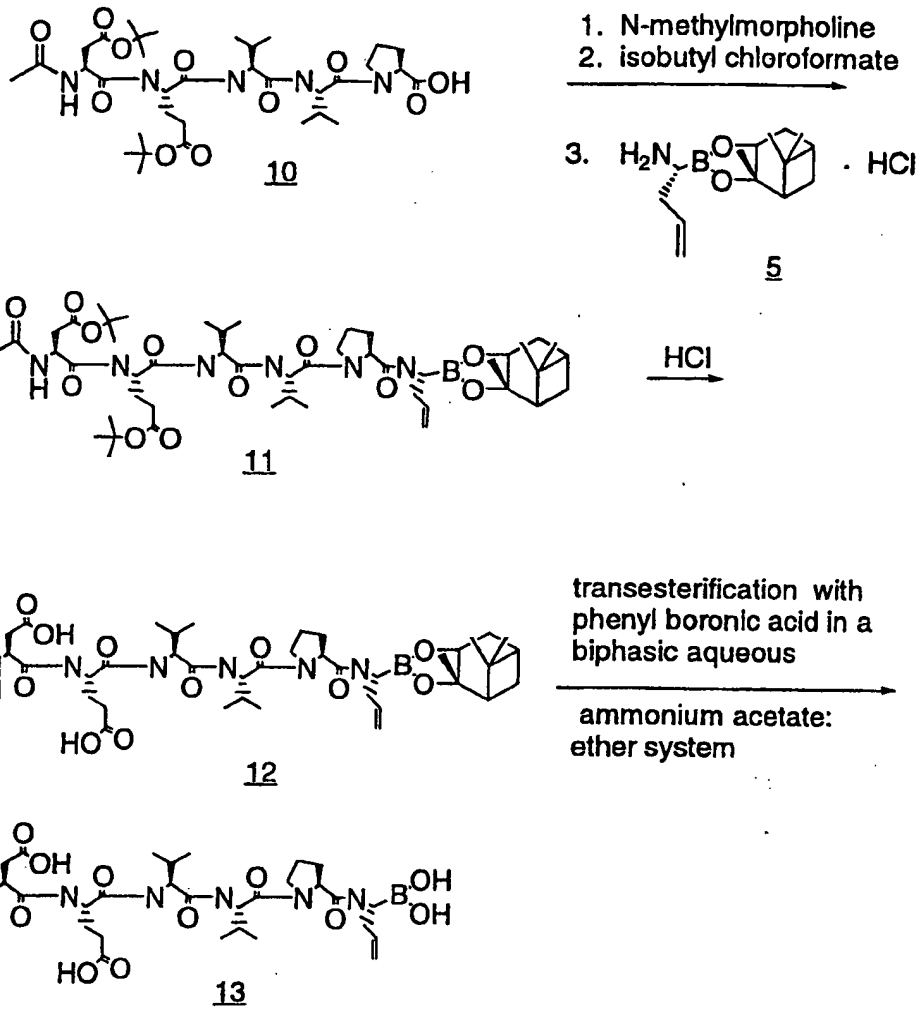
Scheme 2c describes the novel synthesis of boronic acid analogs of cysteine. Vinylmagnisium bromide is allowed to react with triethyl boronate to give vinylboronate diethyl ester. Transesterification with pinanediol gives the corresponding ester **16**. Treatment of **16** with a sulfenyl chloride, for example phenyl sulfenyl chloride, gives the coresponding α-chloro-, α-thiol ether. The α-chloro group is readily converted to the amine using chemistry previously described (Scheme 1). Final deprotection of the thiol is achieved after incorporation of the amine in peptides. Additionally, the treatment of **16** with a thio sulfenyl chloride, for example phenyl thio sulfenyl chloride, followed by conversion to the amine using chemistry previously described (Scheme 1) gives the coresponding α-aminoboronic acid with a substituted disulfide side chain.

Scheme 2c



An acyl group or N-protected peptide with suitable side chain protection is coupled to 5. This method is sufficiently versatile to allow the synthesis of any peptide within the limits normally encountered during peptide synthesis such as insufficient solubility. Acid chlorides or other active forms of acyl groups can be coupled. The preferred method of coupling of protected amino acids and peptides to the α-aminoboronic acids is either the mixed anhydride procedure (Anderson et al., *J. Am. Chem. Soc.* 89, 5012, 1967) or procedures using PyAOP or a related coupling agent (Albericio et al. Tetrahedron Lett. 38, 4853-4856, 1997). This is illustrated in Scheme 3 for the preparation of Ac-Asp-Glu-Val-Val-Pro-boroAlg-OH.

Scheme 3



10

5

11

12

13

In Scheme 3, the mixed anhydride of Ac-Asp(O^tBu)-Glu(O^tBu)-Val-Val-Pro-OH **10** is prepared in THF or DMF by allowing it to react with isobutyl chloroformate in the presence of a N-methylmorpholine or other stericly hindered base. After allowing the reaction to proceed for 5 min at -20°C, **5** is added as a cold solution in either THF or chloroform followed by the addition of a second equivalent of base. The reaction mixture is routinely stirred one hour at -20°C followed by 1-2 h of stirring at room temperature. Insoluble material is removed by filtration,

the solvent removed by evaporation, and the residue dissolved in ethyl acetate. The organic solution is washed with 0.20 N hydrochloric acid, 5% aqueous sodium bicarbonate, and saturated aqueous sodium chloride. The organic phase is then dried over anhydrous sodium sulfate, filtered, and subjected to evaporation. **11** is further purified by techniques known to those skilled the art. These include silica gel chromatography, reverse phase HPLC, and size exclusion chromatography using Sephedex™ LH-20 in methanol.

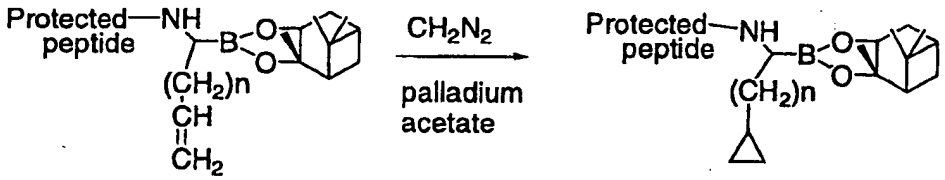
The *tert*-butyl ester protecting groups on Asp and Glu are removed allowing **11** to react with anhydrous HCl to give **12**. The allyl side chain on the boronic acid is compatible with this procedure. A broader range protecting groups can be used for compounds with other side chains. This includes protecting groups that are labile to catalytic hydrogenation. These techniques are known to those skilled in the art and are described in Stewart and Young "Solid Phase Peptide Synthesis" Pierce Chemical Company, (1984).

The boronic acid ester is removed by the procedure described in Kettner US patent 5,384,410 (1995). The boronic acid ester is suspended in ammonium acetate buffer, pH 6.0, and is allowed to react with an excess of phenyl boronic acid added in an equal volume of ether. The product is readily separated from phenyl boronic acid and phenyl boronic acid pinanediol ester by extracting with ether. The free boronic acid, **13**, is obtained by lyophilizing the aqueous phase. Pinanediol esters are also readily removed by treating with anhydrous boron trichloride in methylene chloride as described by Kinder et al., *J. Med. Chem.* **28**, 1917-1925 (1985). The boronic acid ester is treated with a 2-3 fold excess of BCl_3 for 5 min at -78°C and the mixture is allowed to stir 15 min in a 0° ice bath. Excess BCl_3 is hydrolyzed by the slow addition of water. Less structurally rigid boronic acid esters such as pinacol esters can be prepared by transesterification

with diethanolamine and by hydrolyzing the diethanolamine ester with aqueous acid (Kettner and Shenvi *J. Biol. Chem.* 259, 15106-15114, 1984). Compound **13** can be converted to the difluoroborane ($-BF_2$) using a modification of the procedure of Kinder et al., *J. Med. Chem.* 28, 1917-1925 (1985). **13** is treated with a 5-fold molar excess of 0.50 N aqueous hydrofluoric acid at room temperature. Excess hydrofluoric acid and water are removed by lyophilization to give an amorphous white solid.

Scheme 4 shows the synthesis of the cyclopropyl and cyclopropylalkyl side chain inhibitors using the procedure described for the preparation of cyclopropylglycine (Hallinan et al. J. Chem. Soc. Perkin Trans 3537-3543, 1994). The peptide boronic acid containing an unsaturated alkyl sidechain **14** is treated with diazomethane in the presence of palladium acetate to give the product **15**.

Scheme 4



14 15

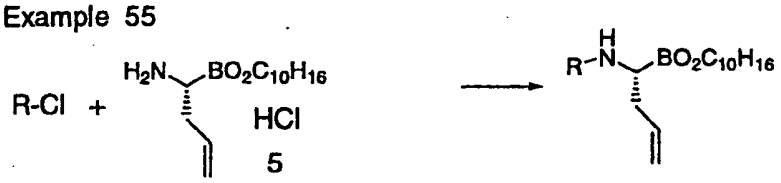
n = 0 or 1

A diverse series of inhibitors is obtained by coupling H-boroAlg-$C_{10}H_{16}$, H-Pro-boroAlg-$C_{10}H_{16}$, H-Leu-boroAlg-$C_{10}H_{16}$, and H-Val-Pro-boroAlg-$C_{10}H_{16}$ to various acyl chlorides and sufonyl chlorides. The acyl chloride or sulfonyl chloride (Aldrich Chem. Co., 25 µmol) was dissolved in 200 µl of ethyl acetate in a screw capped test tube. Either the aminoboronic acids or peptide boronic acids containing a free α-amino group are added followed by Amberlite IRA-068 anion exchange resin (~100 mg). The mixture is heated at

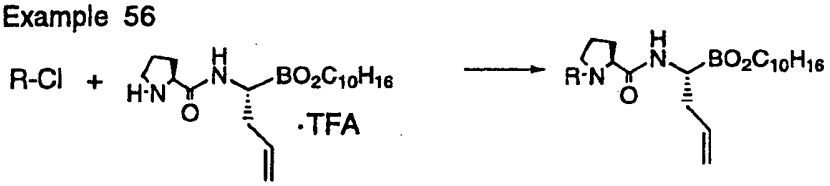
55°C overnight while mixing on an orbital shaker. Water (100 µL) is added and the mixture is shaken an additional 24 h at room temperature. The product is isolated by removing solids by filtration followed by the evaporation of solvent. Compounds were characterized my mass spectral analysis and evaluated as inhibitors of HCV protease. Compounds prepared by this procedure are shown in Tables 2-6. Compounds are characterized by mass spectral analyses and by NMR.

Scheme 5

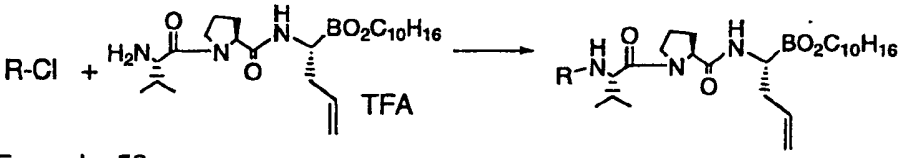
Example 55



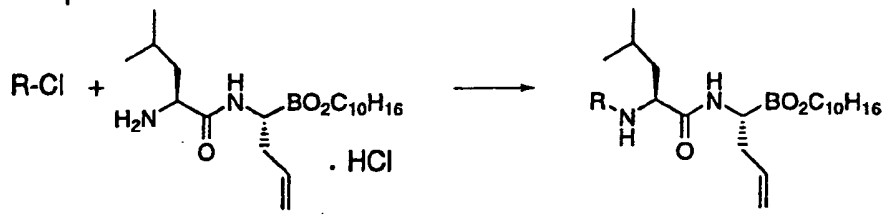
Example 56



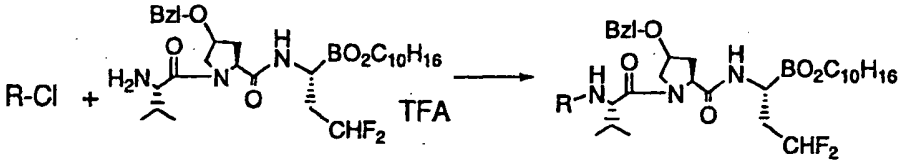
Example 57



Example 58



Example 59



R is either R^4-SO_2- or R^4-CO-

EXAMPLES

The following examples serve to illustrate the invention. Other features of the invention will become apparent in the course of the following descriptions of exemplary embodiments which are given for illustration of the invention and are not intended to be limiting.

Example 1

Preparation of H-boroAlg-pinanediol•HCl (Scheme 1, 4 R=allyl)

2-Propene boronate pinanediol ester. Ether (300 mL) was placed in a 5 L, 4 neck flask equipped with two addition funnels, thermometer and a mechanical stirrer. Triisopropyl borate (Aldrich) (1 mol) in 600 mL of anhydrous ether and allylmagnesium bromide in ether (Aldrich) (1.0 mol, 1.0 L, 1.0 M) were added simultaneously to 300 mL of dry ether at -78^{0}C over a period of 2.5 hours. The mixture was warmed to room temperature and stirred for 12 h. The slurry was recooled to 0^{0}C, followed by dropwise addition of 40 % sulfuric acid (2 mol) over a 1 hour period. The mixture was warmed to room temperature and was allowed to stir for 2 hours. The organic layer was separated and (+)-pinanediol (1.0 mol) was added. After 12 h, the solution was dried over sodium sulfate and filtered. The filtrate was concentrated *in vacuo* and distilled (bp 85-87^{0}C, 1 mm Hg) to give 118 g (53 %) of product as a clear, semi-viscous liquid: ^{1}H-NMR ($CDCl_3$) δ 5.8 - 6.0 (m, 1H), 4.9 - 5.1 (m, 2H), 4.2 (dd, 1H), 2.8 (m, 2H), 2.05-1.78 (m, 6H), 1.38 (s, 3H), 1.27 (s, 3H), 0.83 (s, 3H).

1-Chloro-3-butene boronate pinanediol ester. The α-chloro compound was prepared by homologation of the corresponding allyl boronate. To a 5-liter flask equipped with two addition funnels, thermometer and a mechanical stirrer, was added the allyl boronate (1) (117, 0.53 mol) dissolved in

dry THF (1 L), followed by the addition of cylclohexane (0.5 L) and dichloromethane (0.71 mol). The solution was cooled to -78°C, followed by dropwise addition of lithium diisopropylamide (LDA) in heptane/ THF/ ethylbenzene (0.64 mol, 2.0 M, Aldrich catalog number 36,179-8) over a 1 hour period, taking care that a reaction temperature between -60 to -78°C was maintained. Anhydrous zinc chloride in ether (0.86 mol, 1.0 M) was added. The reaction was warmed to room temperature and stirred for 12 hours. Hexane (600 mL) was added and the mixture was stirred for 1 hour. Cold 1 N H_2SO_4 (3.2 L) was added and the phases were separated. The aqueous layer was washed with hexane (600 mL). The combined organic phases were concentrated to 1 L and washed with 5% sodium bicarbonate (1 L) and saturated sodium chloride (1 L). They were dried over sodium sulfate and filtered. The filtrate was concentrated *in vacuo* and distilled (bp 130-132°C, 0.5 mm Hg) to give 60 g (42 %) of the α-chloroboronic acid as a clear yellow oil. ^{1}H-NMR ($CDCl_3$) δ 5.8 - 6.0 (m, 1H), 5.2 (m, 2H), 4.2 (dd, 1H), 3.48 (q, 1H) 2.8 (m, 2H), 2.05-1.78 (m, 6H), 1.41 (s, 3H), 1.29 (s, 3H), 0.84 (s, 3H).

H-boroAlg pinanediol ester•hydrochloride . The *bis*-trimethylsilane protected amine (**3**, Scheme 1) was prepared by dissolving hexamethyldisilizane (64.4 mmol) in dry THF (30 mL) and cooling to -78°C. *n*-Butyl lithium in hexane (1.6 N, 70.8 mmol) was added and the solution was allowed to warm to room temperature. It was recooled to -78°C and 1-chloro-3-butene boronate pinanediol (17.2 g, 64.4 mmol) was added in 30 mL THF. The mixture was allowed to slowly warm to room temperature and to stir overnight. Solvent was removed by evaporation and dry hexane (200 mL) was added. Insoluble material was removed by filtration under a nitrogen atmosphere through a bed of celite to yield a solution of the protected amine. This solution was cooled to -78°C and 4 N anhydrous hydrogen chloride in dioxane (192 mmol) was added. The reaction was slowly allowed to

warm to room temperature and to stir overnight. The solvent was evaporated under vacuum to yield a brown oil. It was purified on a 5 x 90 cm column of Sephadex™ LH-20 in methanol. TLC in ethyl acetate:hexane (1:1) indicated the product as a single base spot which gave a positive test for amines after spraying with ninhydrin. The product eluted in fractions 51-70 (10mL fractions). The fractions were pooled, concentrated, and dried under vacuum to give 16 g (87.2%) of the desired product as a foam. ^{1}H-NMR ($CDCl_3$) δ 8.21 (bs, 2H), 5.80 - 6.0 (m, 1H), 5.20 (m, 2H), 4.2 (dd, 1H), 3.0 (m, 1H), 2.62 (m, 2H), 2.4 - 1.78 (m, 6H), 1.41 (s, 3H), 1.29 (s, 3H), 0.80 (s, 3H).

EXAMPLE 2

Preparation of boroAbu-pinanediol ester (Scheme 1, 4 R=ethyl)

Propane boronate pinanediol ester. The alkyl boronate was prepared on a 0.50 mole scale using a procedure similar to the one used in the preparation of allyl boronate pinanediol. The crude product was distilled (bp 63°C, 2 mm Hg) to give 32.3 g (41.4 %) of 6 as a clear oil. ^{1}H-NMR ($CDCl_3$) δ 4.23 (dd, 1H), 2.40-1.78 (m, 6H), 1.38 (s, 3H), 1.28 (s, 3H), 0.97 (t, 3H), 0.83 (s, 3H), 0.79 (q, 2H).

1-Chloropropane boronate pinanediol ester. The α-chloro boronic acid was prepared on a 0.21 mole scale by the procedure described for Example 1 except the reaction mixture was washed with saturated aqueous ammonium chloride (1000 mL) rather than sulfuric acid. Phases were separated and the aqueous layer was washed with an equal volume of hexane. The organic phases were combined, dried over anhydrous sodium sulfate, filtered and concentrated to give a crude product which was distilled (bp 100-102°C, 0.6 mm Hg) to yield 28.8g (54.4 %) of the desired product as a clear yellow oil. ^{1}H-NMR ($CDCl_3$) δ 4.35 (dd, 1H), 3.41

(m, 1H), 2.40-1.80 (m, 8H), 1.41 (s, 3H), 1.29 (s, 3H), 1.02 (t, 3H), 0.84 (s, 3H).

H-boroAbu pinanediol ester•hydrochloride. The amino boronic acid was prepared on a 0.09 mole scale and was purified by a procedure similar to the one described for Example 1 to yield 23 g of crude product. A proportion of this material (13 g) was purified by chromatography on an LH-20 column to give 7.47 g (54.9 %)of the desired product as a brown foam. ^{1}H-NMR ($CDCl_3$) δ 8.24 (s, 3H), 4.36 (dd, 1H), 2.91 (m, 1H), 1.8-2.4 (m, 8H), 1.41 (s, 3H), 1.27 (s, 3H), 1.08 (t, 3H), 0.82 (s, 3H).

Example 3

Preparation of boro-Cyclopropylglycine pinacol ester (Scheme 1, R= cyclopropyl)

Cyclopropylboronate pinacol ester . The pinacol cyclopropyl bornate ester was prepared by the addition of cyclopropyl magnesium bromide was added to isopropylboronate pinacol ester. The latter compound was prepared by a previously described procedure (Andersen, M. W.; Hildebrandt, B.; Koster, G.; Hoffmann, R. W. *Chem. Ber.* **122**, *1989*, 1777-1782). The Grignard reagent was prepared by adding cyclopropylbromide (3.0 mL, 37 mmol) to magnesium turnings (11 g, 0.46 mole) in THF (300 mL) at room temperature under nitrogen. The solution was carefully warmed to 42°C at which point a vigorous exotherm ensued. After the exotherm had subsided an additional 3 mL of cyclopropylbromide was added and an exotherm ensued and subsided. This iterative process was repeated until all of the cyclopropyl bromide was added (36 mL, 0.45 mole). The solution was heated at 50°C for an additional 2 h. At this time the contents of the flask were transferred to an addition funnel and added to a solution of isopropylboronate pinacol ester (84 g, 0.45 mol) in ether (400 mL) in a 3-necked, 2-liter flask in ether (500 mL) at

-78°C under nitrogen. The cyclopropyl Grignard reagent was added dropwise over a period of 3 h. The solution was allowed to warm to room temperature and stirred overnight. The solution was cooled to 0°C and 1 N HCl prepared in saturated aqueous NaCl (500 mL) was added dropwise over a period of 1 h. The solution was allowed to stir for an additional 4 h and the layers were separated. The aqueous layer was extracted with hexanes (3 x 300 mL), dried over $MgSO_4$, and concentrated using a rotary evaporator. The residue was purified by silica gel chromatography using 10% ethyl acetate: hexanes as a solvent to yield a clear colorless oil (42 g, 0.25 mole, 56%), bp 50-52°C, 8 mm Hg. ^1H NMR d 0.36-0.50 (m, 5H), 1.18 (s, 12H).

1-Chloro-1-cyclopropylmethyl boronate pinacol ester. A 3-necked 250 mL flask containing THF (75 mL) and dichloromethane (2.5 mL, 39 mmol) was cooled to -100°C. *n*-Butyllithium (1.6 M in Hexanes, 24 mL, 39 mmol) was added cautiously to maintain a solution temperature of -100°C. After stirring at -100°C for 45 min, a solution of cyclopropylboronate pinacol ester (6.0 g, 36 mmol) in THF (10 mL) precooled to -78°C was added. The solution was allowed to warm to room temperature and stirred for an additional 12 h. The solution was concentrated by evaporation and hexanes were added to give a solid. The mixture was filtered and the filtrate was evaporated to give an oil. This material was distilled through a short path distillation apparatus (67-70°C, 0.2 mm Hg) to yield a clear colorless oil (5.5 g, 58 % yield). ^1H-NMR d ($CDCl_3$) 2.87 (d, 2H), 1.27 (s, 12H), 0.63 (m, 3H), 0.37 (m, 2H).

H-boroCyclopropylglycine pinanediol ester. The α-chloro compound (5.0 g, 23 mmol) was dissolved in THF (50 mL) and added to a freshly prepared solution of lithium *bis*-trimethylsilylamide (100 mL of a 3.2 M solution) at -78°C under nitrogen. The solution was warmed to room temperature and stirred for 18 h. THF was removed by

rotary evaporation and hexanes were added to the oil to give a precipitate. The solid was removed by filtration and the filtrate was cooled to -78°C. A solution of 4 N HCl in dioxane (17 mL, 69 mmol, 3 equivalents) was added and the solution was stirred for 4 h while warming to room temperature to yield a solid. It was isolated by filtration and dissolved in hot $CHCl_3$ (150 mL). Following concentration to 10 mL, hot ethyl acetate (~25 mL) was added. Slow crystallization gave the desired product (3.3 g, 14 mmol, 60% yield). ^1H NMR ($CDCl_3$) 8.22 (br. s, 3H), 3.47 (m, 1H), 1.28 (s, 12H), 0.65 (m, 4H), 0.38 (m, 1H).

Example 4

Preparation of H-borodifluoroethylglycine pinanediol (Scheme 2, R= 2,2-difluoroethyl)

Chloromethyl boronate pinacol ester. Tetrahydrofuran (150 mL) was placed in a 1 L, 3 neck flask equipped with two addition funnels. Triisopropyl borate (Aldrich) (32.1 mL, 139 mmol) and chloro-iodomethane (Aldrich) (10.3 mL, 142 mmol) were added to the flask. The reaction mixture was cooled to -78°C. *n*-Butyllithium (81.9 mL, 131 mmol, 1.6 M in hexanes) was added dropwise to the flask via an addition funnel. The solution was stirred at -78°C for 2 hours and then gradually warmed to -10°C. A crystal of methyl orange was added to the reaction. Hydrogen chloride (1.0 N in ether) was added via the other addition funnel until the methyl orange end point was reached. Pinacol (16.4g, 139 mmol) was added to the flask and the reaction mixture was stirred for 12 hours. It was then concentrated *in vacuo* and distilled (bp 61-63°C, 5 mm Hg) to give 16.0 g (65 %) of the desired compound as a yellow oil. ^1H NMR ($CDCl_3$) δ 2.97 (s, 2H, $ClCH_2B$), 1.29 (s, 12H, CCH_3).

Iodomethyl boronate pinacol. THF (800 mL) was placed in a 3 L, 3-necked flask equipped with two addition funnels. Triisopropyl boronate (Aldrich) (128 mL, 0.55 mol) and

chloro-iodomethane (Aldrich) (100 g, 0.56 mol) were added. The mixture was cooled to -78°C and n butyl lithium (330 mL, 0.53 mol, 1.6 M in hexanes) was added dropwise. The solution was stirred for 2 hand slowly allowed to warm to -10°C. Methyl orange indicator was added and HCl (1.0 M in ether) was added until the methyl orange endpoint was reached. Pinacol (65 g, 0.55 mol) was added and reaction mixture was allowed to stir 12 h. It was filtered and evaporated in vacuo. The residue was dissolved in acetone (500 mL) and sodium iodide (70 g, 0.47 mol) was added. After stirring for 12 h at room temperature, solvent was removed by evaporation and the residue was dissolved in ethyl acetate and washed with saturated aqueous NaCl. The organic phase was dried over Na_2SO_4, filtered, and concentrated in vacuo. It was distilled to give 69 g (47%) of the desired product (bp 45-50°C, 1.5 mm). ^1H NMR ($CDCl_3$) δ 2.16 (s, 2H), 1.26 (s, 12H).

Phenylthiomethane boronate pinacol ester. Thiophenol (11.6 mL, 113 mmol) was dissolved in DMF (40 mL) and diisopropylethylamine (19.8 mL, 113 mmol) and chloromethyl boronate pinacol ester (20 g, 113 mmol) were added sequentially. (Iodomethyl boronate pinacol can be readily substituted for the chloro compound.) After stirring for 12 hours, solvent was removed by rotary evaporation and ether (70 mL) was added. The reaction mixture was washed with 0.2 N HCl (70 mL), 5 % $NaHCO_3$ (70 mL) and saturated sodium chloride (70 mL). The combined organic phases were dried over sodium sulfate and filtered. The filtrate was concentrated *in vacuo* and distilled (bp 125-127°C, 0.6 mm Hg) to give 21.6 g (76 %) of the desired product as a clear oil. ^1H NMR ($CDCl_3$) δ 7.32 - 7.11 (m, 5H), 2.42 (s, 2H), 1.24 (s, 12H).

1-Phenylthio-3,3-difluoropropane-1-boronate pinacol ester. Butyllithium (50.6 mL, 126 mmol, 2.5 M in hexanes) was

added dropwise to a solution of diisopropylamine (18.4 mL, 133 mmol) dissolved in THF (40 mL) at 0°C in a 500 mL round bottom flask. A solution of phenylthiomethane boronate pinacol ester (31.6 g, 126 mmol) in THF (40 mL) was added dropwise over a period of approximately 2 min to yield a white precipitate. After stirring for 1 hour at 0°C, 1,1-difluoro-2-bromoethane (Lancaster) (51 mL, 630 mmol) was added dropwise. The precipitate dissolved and the solution was allowed to warm to room temperature and stirred for 16 hours. Excess cold 10 % phosphoric acid was added and the mixture was stirred for 5 min. Ether (100 mL) was added and the phases were separated. The organic layer was dried over sodium sulfate and filtered. The filtrate was concentrated *in vacuo* and distilled (bp 119-122°C, 0.4 mm Hg) to give 22 g (56 %) of product as a clear oil. ^{1}H NMR ($CDCl_3$) δ 7.43 - 7.19 (m, 5H, C_6H_5), 6.16 - 5.78 (tt, 1H, CHF_2), 2.82 (m, 1H, SCHB), 2.38 - 2.19 (m, 2H, $C\underline{H}_2CHF_2$), 1.23 (s, 12H, CCH_3). ^{19}F NMR δ -116.8 to -117.0 (dt, CHF_2).

1-Iodo-3,3-difluoropropane-1-boronate pinacol ester. 1-Phenylthio-3,3-difluoropropane-1-boronate pinacol ester (6.00 g, 19.1 mmol) was dissolved in anhydrous acetonitrile (60 mL) and dry methyl iodide (24 mL, 380 mmol) and sodium iodide (5.76 g, 38.2 mmol) were added. The reaction mixture was vigorously refluxed for 5 h. The solvent was evaporated *in vacuo*. The residue was partitioned between water (40 mL) and ether (40 mL). The phases were separated and the organic phase was washed with an equal volume of ether. The combined organic phases were dried over Na_2SO_4 and evaporated to give a brown oil which was purified by distillation to give 3.1 g (49%), bp 63-65°C, 0.4 mm. ^{1}H NMR ($CDCl_3$) δ 6.18 - 5.79 (tt, 1H, CHF_2), 3.21 (t, 1H, ICHB), 2.43 - 2.21 (m, 2H, $C\underline{H}_2CHF_2$), 1.27 (s, 12H, CCH_3).

1-Amino-3,3-difluoropropyl boronate pinacol•HCl. 1-Iodo-3,3-difluoropropanyl boronate pinacol (2.7 g, 8.1 mmol) was dissolved in THF (10 mL) and was added dropwise to a solution of lithium bis(trimethylsilyl)amide (9.68 mL, 9.68 mmol, 1.0 M in THF) dissolved in anhydrous THF (10 mL) and cooled to -78°C. The reaction mixture was allowed to warm to room temperature and stirred for 12 h. It was concentrated *in vacuo* and hexane was added. The reaction mixture was cooled to -78°C, followed by the dropwise addition of 4 N anhydrous hydrogen chloride in dioxane (6.05 mL, 24.2 mmol). The mixture was allowed to warm to room temperature and stirred for 5 hours. The reaction mixture was evaporated and chloroform was added. Insoluble material was removed by filtration. The filtrate was evaporated almost to dryness and hexanes were added. Upon standing the product crystallized. It was isolated and washed with cold hexane to yield 1.1 g (52 %), mp 138-141°C. ^{1}H NMR ($CDCl_3$) δ 7.68 (bs, 3H), 6.22 - 6.01 (tt, 1H), 3.42 (m, 1H), 2.76 - 2.51 (m, 2H), 1.32 (s, 12H). ^{19}F NMR δ -115.2 to -115.5 (dt, CHF_2). HRMS calculated for $C_9H_{18}B_1O_2F_2N$ +H: 222.1. Found: 222.1.

Example 5a

Preparation of boroVinylglycine pinanediol (NH_2-$CH(CH=CH_2)BO_2C_{10}H_{16}$•HCl)

1-Chloro-1-vinylmethyl boronate pinanediol. The α-chlorovinyl compound was prepared by the method described by Matteson, D.S. & Majumdar, D. *Organometallics* **2**, 1529-1535, 1983.

boro-Vinylglycine pinanediol Ester•HCl . The α-chlorovinyl boronate pinanediol ester (10.6 g, 41.7 mmol) was dissolved in THF (100 mL) and added to a freshly prepared solution of lithium hexamethyldisilazide (45.9 mmol) in THF (150 mL) at -78°C. This solution was stirred for 20 h while warming to

room temperature. THF was removed *in vacuo* and hexanes (150 mL) were added. The resulting precipitate was removed by filtration. The filtrate was cooled to - 78°C and a solution of HCl in dioxane (4.0 N, 31.3 mL, 125 mmol) was added. The solution was allowed to warm to room temperature and to stir for 20 h. The solvents were removed in vacuo to yield 7.2 g (26 mmol, 63 % yield) of a bright orange, viscous oil which formed a glass when placed under high vacuum. ^{1}H-NMR ($CDCl_3$) d 0.76 (s, 3H), 1.21 (s, 3H), 1.36 (s, 3H), 1.83-2.25 (m, 6H), 3.64 (d, 2H), 4.34 (d, 1H), 5.24 (d, 1H), 5.45 (d, 1H), 5.97 (m, 1H), 8.47 (br. s, 3H).

Example 5b

Preparation of H-boroThreonine(OBzl)-pinanediol

Pinacol (1-chloroethyl)boronate. A 250 mL round bottom flask is charged with THF (60 mL) and CH_2Cl_2 (2.63 mL, 41.0 mmol). The solution was cooled to - 100°C with a liquid nitrogen/methanol/H_2O bath. *n*-BuLi (1.6 N in hexanes, 25.7 mL) was added slowly over the course of 1 h. The resulting solution was stirred for an additional 45 min at -100°C. Pinacol methyl boronate, dissolved in THF (40 mL), was added and the solution was stirred overnight while warming to room temperature. The THF was removed by evaporation and hexanes (100 mL) were added. The resulting precipitate was filtered and the solution concentrated. The residue was distilled at 70°C, 2 mm Hg to yield 2.06 g (30 %) of a clear colorless oil. ^{1}H-NMR ($CDCl_3$) δ 3.49 (q, 1H), 1.52 (d, 4H), 1.27 (s, 12H).

Pinanediol (1-benzyloxyethyl)boronate. *n*-BuLi (1.6 N, 13.8 mL) was added to a solution of benzyl alcohol (2.3 mL, 22 mmol) in THF (60 mL) at -78 °C followed by DMSO (1.6 mL, 22 mmol). The solution was allowed to warm to room temperature and stir for 1 h. The solution was recooled to

0°C and a solution of Pinacol (1-chloroethyl)boronate (2.06 g, 11 mmol) in THF (60 mL) was added. The solution was stirred at room temperature for 1 h and then heated at 60°C for 5 h. The contents of the flask are poured into 0.2 N HCl (300 mL). The layers were separated and the aqueous layer was washed with ether (3 x 100 mL). The combined organic layers were washed with brine and dried over Na_2SO_4. To this solution was added (s)-pinanediol (1.87 g, 11.0 mmol) and the solution was stirred for 1 day and concentrated to yield an oil. This oil was purified by silica gel column chromatography using 10% ethyl acetate/90% hexane as an eluent. The appropriate fractions are pooled and the solvent evaporated to yield 2.66 g (77% yield) of a pale yellow oil. ^{1}H-NMR ($CDCl_3$) δ 7.30 (m, 5H), 4.57 (s, 2H), 4.32 (d, 1H), 3.45 (dq, 1H), 2.39-1.82 (m, 6H), 1.41 (s, 3H), 1.40 (dd, 3H), 1.29 (s, 3H), 0.84 (s, 3H).

Pinanediol (2-benzyloxy-1-chloropropyl)boronate. CH_2Cl_2 (0.80 mL, 12.7 mmol) was added to THF (40 mL) and cooled to -100°C. *n*-BuLi (1.6 N, 6.3 mL) was slowly added while maintaining a temperature of -100°C. The flask was stirred at -100°C for an additional 45 min. Pinanediol (1-benzyloxyethyl)boronate (2.66 g, 8.46 mmol), dissolved in THF (20 mL), was added followed by a solution of zinc(II) chloride in ether (1.0 N, 17 mL). The THF was evaporated and the residue was redissolved in hexanes (150 mL). The solution was washed with saturated aqueous ammonium chloride, brine, and dried over $MgSO_4$. It was concentrated to give a light oil. This oil was purified by silica gel column chromatography (10% ethyl acetate/90% hexanes eluant) to yield 1.55 g (51%) of a clear oil. ^{1}H-NMR ($CDCl_3$) δ 7.36 (m, 5H), 4.58 (m, 2H), 4.37 (d, 1H), 3.91 (m, 1H), 3.56 (d, 2H), 2.39-1.81 (m, 6H), 1.40 (d, 3H), 1.34 (d, 3H), 1.29 (s, 3H), 0.84 (s, 3H).

Pinanediol (2-benzyloxy-1-aminopropyl)boronate•HCl.

Pinanediol (2-benzyloxy-1-chloropropyl)boronate, dissolved (3.85 g, 10.6 mmol)) in THF (60 mL), was added to a solution of LiHMDS (10.6 mmol) in THF at -78°C. The solution was stirred for 1 h at -78°C and allowed to warm to room temperature. Solvent was evaporated and the residue redissolved in hexanes (120 mL). The solid was filtered and the filtrate recooled to -78°C, and a solution of HCl in 1,4-dioxane (4 N, 8.0 mL) was added. The solution was allowed to warm to room temperature while stirring overnight. The solvent was evaporated to yield 2.55 g (63%) of a brown oil. ^{1}H-NMR ($CDCl_3$) d 8.11 (br s, 3H), 7.35 (m, 5H), 4.57 (m, 2H), 4.32 (m, 1H), 3.16 (br s, 1H), 2.34-1.83 (m, 6H), 1.38 (s, 3H), 1.33 (m, 3H), 1.24 (s, 3H), 0.79 (s, 3H).

Example 5c

Preparation of H-boroSer(OBzl)-pinanediol HCl.

H-boroSer(OBzl)-pinanediol HCl was prepared by adding Pinanediol 1-chloro-2-benzyloxy-boronate (5.0g, 14.3 mmol) in THF (60 mL) to a solution of LiHMDS (15 mmol) in THF (60 mL) at -78°C. The solution was allowed to stir while warming to room temperature over a period of 3 h. The THF was evaporated, the residue redissolved in anhydrous hexanes (200 mL), cooled to -78°C, and a solution of HCl in dioxane (4 N, 11.3 mL) was added. The resulting mixture was allowed to stir while warming to room temperature. The solids were removed by filtration. The filtrate was evaporated and triturated with chloroform (50 mL) and refiltered. The chloroform was evaporated and the residue dissolved in hot hexanes (30 mL). As the hexanes were allowed to cool a cream colored solid crystallized. This solid was combined with a solid that had crystallized from the original hexanes filtrate. The combined solids were filtered, dried in vacuo to yield 2.4 g (46%) of a cream colored solid, mp 112-115°C. ^{1}H-NMR ($CDCl_3$) 8.16 (br s.,

3H), 4.59 (dd, 2H), 4.37 (d, 1H), 4.02 (m, 1H), 3.83 (m, 1H), 3.31 (br s, 1H), 2.31-2.11 (m, 2H). 2.02 (t, 1H), 1.91-1.84 (m, 3H), 1.39 (s, 3H), 1.25 (s, 3H), 0.79 (s, 3H). MS/ESI calculated for $C_{19}H_{29}BNO_3$ + H^+: 330.2: Found: 330.3.

Example 5d

Preparation of Pinanediol 1-amino-2-thiophenylethylboronate HCl.

Pinanediol 1-chloro-2-thio(phenyl)ethylboronate.

Phenylsulfenyl chloride (2.0 g, 13.8 mmol) was added to a solution of pinanediol vinyl boronate (2.85 g, 13.8 mmol) in CH_2Cl_2 (30 mL). The solution was stirred for 30 min and then the solution was evaporated to yield 3.9 g (81%) of a pale yellow oil. ^{1}H-NMR ($CDCl_3$) δ 7.40 (m, 5H), 4.40 (d, 1H), 3.49 (m, 1H), 3.64 (m, 1H), 3.33 (m, 2H), 2.34-1.89 (m, 6H), 1.43 (s, 3H), 1.30 (s, 3H), 0.85 (s, 3H). MS/APCI calculated for $C_{18}H_{24}BClO_4S$ + H: 351.I. Found: 351.0.

Pinanediol 1-amino-2-thiophenylethylboronate HCl.

Pinanediol 1-chloro-2-thio(phenyl)ethylboronate (2.0 g, 5.7 mmol) dissolved in THF (40 mL) was added to a solution LiHMDS (6.0 mmol) in THF (60 mL) at -78°C. The solution was allowed to warm to room temperature and solvent was evaporated. The residue was redissolved in hexanes, filtered and recooled to -78°C. A solution of HCl in dioxane (4 N, 5 mL) was added and the mixture was allowed to stir overnight while warming to room temperature. The solvent was removed to yield 1.2 g (57%) of the desired product as a yellow foam. ^{1}H-NMR δ 8.46 (br s, 3H), 4.33 (d, 1H), 3.75 (s, 3H), 3.48 (br s, 2H), 3.15 (m, H), 2.4-1.8 (m, 6H), 1.35 (s, 3H), 1.23 (s, 3H), 0.78 (s, 3H). MS/ESI calculated for $C_{18}H_{27}BNO_2S$: 332.3. Found: 332.2.

Example 5e

Pinanediol 1-amino-2-thiolsulfenyl(phenyl)ethyl boronate

1-Chloro-2-thiolsulfenyl(phenyl)ethyl boronate pinanediol. Phenylthiosulfenyl chloride was prepared by reacting benzene thiol with sulfur dichloride at -78°C using a published procedure (Can. J. Chem., 51, 3403-3412, 1973). 1-Chloro-2-thiolsulfenyl(phenyl)ethyl boronate pinanediol was obtained by adding phenylthiosulfenyl chloride (3.2 g, 18.2 mmol) dissolved in dichloromethane (30 mL) dropwise over a period of 10 min to a solution of pinanediol vinylboronate (3.7 g, 18.2 mmol) in CH_2Cl_2 (50 mL) in the presence of $CaCO_3$ (30 mg). The resulting solution was stirred for an additional 1 h at room temperature. The contents of the flask were poured into brine (100 mL), the layers were separated and the organic layer was dried over Na_2SO_4. The organic layer was evaporated to yield a pale, yellow-green oil which was further purified by silica gel column chromatography (eluant 1% EtOAc/99% Hexanes). The appropriate fractions were pooled and evaporated to yield 2.93 g (7.8 mmol, 43%) of a pale green viscous oil. MS/APCI calculated for $C_{18}H_{24}BClO_2S_2$ + H: 383. Found: 383. ^{1}H-NMR $CDCl_3$ δ 0.85 (s, 3H), 1.30 (s, 3H), 1.42 (s, 3H), 1.86-2.40 (m, 6H), 3.11-3.32 (m, 2H), 3.73 (t, 1H), 4.37 (dd, 1H), 7.22-7.63 (m, 5H).

Pinanediol 1-amino-2-thiolsulfenyl(phenyl)ethyl boronate. 1-Chloro-2-thiolsulfenyl(phenyl)ethyl boronate pinanediol was treated with lithium hexamethyldisilane by the procedure in Example 5d to yield the alpha-amino compound. MS/ESI calculated for $C_{18}H_{26}BNO_2S_2$ + H: 364. Found: 364.

Example 5f

Preparation of Pinacol 1-amino-3,3,3-trifluorobutyl boronate

1-Phenylthio-4,4,4-trifluorobutane-1-boronate pinacol ester. Phenylthiomethane boronate pinacol ester was prepared by the procedure in Example 4. Diisopropylamine (4.7 ml, 33.6 mmol) was dissolved in THF (10 mL) and stirred at 0 °C in a 100 mL round bottom flask. Butyllithium (12.8 mL, 32.0 mmol, 2.5M in hexanes) was added dropwise to the solution. A solution of phenylthiomethane boronate pinacol ester (8.0 g, 32.0 mmol) in THF (10 mL) was added dropwise rapidly, yielding a white precipitate. The reaction mixture was stirred for 1 hour at 0 °C, followed by the dropwise addition of 3,3,3-trifluoropropyl iodide (Lancaster) (15.0g, 64.0 mmol). The precipitate dissolved and the solution was allowed to warm to room temperature and stirred for 12 hours. The mixture was then treated with excess cold 10 % phosphoric acid and stirred for 5 minutes. The reaction mixture was poured into a separatory funnel and extracted with ether (100 mL). The organic layer was dried over sodium sulfate and filtered. The filtrate was concentrated *in vacuo* and distilled (bp 112-114 °C, 0.25 mm Hg) to give 6.53g (59 %) of the desired product as a clear oil. ^{1}H nmr ($CDCl_3$) δ 7.41 - 7.11 (m, 5H, C_6H_5), 2.78 (t, 1H, SCHB), 2.35 (m, 2H, $C\underline{H_2}CF_3$), 1.98 (m, 1H, $C\underline{H_2}C\underline{H_2}CF_3$), 1.23 (s, 12H, CCH_3). ^{19}F nmr δ -116.8 to -117.0 (t, 3H, CF_3).

1-iodo-4,4,4-trifluorobutane-1-boronate pinacol ester. 1-Phenylthio-4,4,4-trifluorobutane-1-boronate pinacol ester (3.3g, 9.5 mmol) was dissolved in anhydrous acetonitrile (33 mL). Dry methyl iodide (11.9 mL, 190.6 mmol) was added, followed by the addition of sodium iodide (2.87g, 19.1 mmol). The reaction mixture was refluxed for 12 h. The solvent was evaporated to give an oily residue which was purified by distillation to give 3.32g (95.6 %), bp 51 °C, 0.5 mm Hg. ^{1}H nmr ($CDCl_3$) δ 3.21 (t, 1H, ICHB), 2.39 (m, 2H, $C\underline{H_2}CF_3$), 2.05 (m, 2H, $C\underline{H_2}C\underline{H_2}CF_3$), 1.27(s, 12H, CCH_3).

1-amino-4,4,4-trifluorobutyl boronate pinanediol ester. 1-iodo-4,4,4-trifluorobutyl pinacol ester (3.4g, 9.58 mmol) was dissolved in THF (20 mL) and was added dropwise to a solution of lithium bis(trimethylsilyl)amide (Aldrich) (9.6 ml, 9.6 mmol, 1.0M in THF) dissolved in anhydrous THF (20 ml and cooled to -78 °C). The reaction mixture was allowed to warm to room temperature and stirred for 12 hours. It was concentrated *in vacuo* and hexane was added. The reaction mixture was cooled to -78 °C and 4M anhydrous hydrogen chloride in dioxane (7.2 ml, 28.7 mmol) was added dropwise. The solution was allowed to warm to room temperature and stirred for 3 hours. The reaction mixture was concentrated and chloroform was added. Insoluble material was removed by filtration. The filtrate was evaporated almost to dryness and hexanes were added. Upon standing the product crystallized. It was isolated and washed with cold hexanes to yield 1.7g (69.8 %) of a brown solid. ^{1}H nmr ($CDCl_3$) δ 7.80 (bs, 3H), 3.19 (m, 1H), 2.78 (m, 1H), 2.58 - 2.05 (m, 3H), 1.23 (s, 12H). ^{19}F nmr ($CDCl_3$) δ -66.67 to -66.59 (t, 3H, CF_3).

Example 5g

Preparation of H-boroAsp(O^tBu)$C_{10}H_{16}$.

1-Phenylthio-2-*t*-butoxycarbonylethane-1-boronate pinacol ester. Phenylthiomethane boronate pinacol ester was prepared the procedure described for Example 4. Diisopropylamine (5.8 ml, 42.0 mmol) was dissolved in THF (20 ml) and stirred at 0°C in a 500 ml round bottom flask. *n*-Butyllithium (16.0 ml, 40.0 mmol, 2.5M in hexanes) was added dropwise to the solution. A solution of phenylthiomethane boronate pinacol ester (10.0g, 40.0 mmol) in THF (20 ml) was added dropwise rapidly, yielding a white precipitate. The reaction mixture was stirred for 1 hour at 0°C, followed by the dropwise addition of *tert*-butyl bromoacetate (Aldrich) (17.7 ml, 120 mmol). The precipitate dissolved and the solution was allowed to warm

to room temperature and stirred for 16 hours. The mixture was then treated with excess cold 10 % phosphoric acid and stirred for 5 minutes. The reaction mixture was poured into a separatory funnel and extracted with ether (100 ml). The organic layer was dried over sodium sulfate and filtered. The filtrate was concentrated *in vacuo* and purified by silica gel eluting with 10 % ethyl acetate: hexanes as a solvent to yield a clear colorless oil (4.77 g, 0.014 mol, 34.9%). ^{1}H NMR ($CDCl_3$) δ 7.43-7.19 (m, 5H), 2.98 (t, 1H), 2.62 (d, 2H), 1.41 (s, 9H), 1.25 (d, 12H).

1-iodo-2-*t*-butoxycarbonylethyl-1-boronate pinacol ester. 1-Phenylthio-2-*t*-butoxycarbonylethane-1-boronate pinacol ester (0.76 g, 2.09 mmol) was dissolved in anhydrous acetonitrile (10 ml). Dry methyl iodide (2.62 ml, 41.8 mmol) was added, followed by the addition of sodium iodide (0.15 g, 4.18 mmol). The reaction mixture was refluxed for 8 hours. The solvent was evaporated *in vacuo*. Water (20 ml) was added and the crude product was extracted into ether (20 ml). It was dried over MgSO4 and concentrated using a rotary evaporator. The crude mixture was purified by silica gel chromatography using 40 % ethyl acetate: hexanes to yield a brown oil (0.25 g, 0.66 mmol, 31 %). ^{1}H NMR ($CDCl_3$) δ 3.38 (t, 1H), 2.8 (m, 2H), 1.41 (s, 9H, CCH_3), 1.24 (d, 12H).

1-azido-2-*t*-butoxycarbonylethane-1-boronate pinacol ester. To a solution of tetrabutylammonium bromide (0.053 g, 0.16 mmol), dissolved in dichloromethane (60 ml), was added a solution of sodium azide (2.11g, 32.2 mmol) dissolved in water (16 ml). The reaction mixture was vigorously stirred as 1-iodo-2-*t*-butoxycarbonylethyl-1-boronate pinacol ester, dissolved in dichloromethane (13 ml), was added dropwise. The reaction was stirred for 10 hours. After removing solvent by evaporation, saturated ammonium chloride was added and the product was extracted into dichloromethane (30 ml). It was dried over $MgSO_4$ and concentrated using a rotary evaporator to give yellow oil.

^{1}H NMR ($CDCl_3$) δ 3.35 (t, 1H), 2.60 (d, 1H), 1.43 (s, 9H), 1.27 (s, 12H).

1-azido-2-*t*-butoxycarbonylethane-1-boronate pinanediol ester. The pinacol ester (0.90 g, 3.0 mmol) was dissolved in THF (5 ml) and pinanediol (0.56 g, 3.3 mmol) was added. After stirring for 2 hours, solvent was evaporated and the residue purified by silica gel chromatography using 95 % hexanes: ethyl acetate. The product was obtained as a light brown oil (0.62 g, 1.76 mmol, 58 %). TLC in hexanes: ethyl acetate (17:3) indicated a single spot, R_F 0.43. ^{1}H NMR ($CDCl_3$) δ 4.2 (tt, 1H), 3.41 (m, 1H), 2.61 (m, 2H), 2.40-1.85 (m, 6H), 1.43 (s, 9H), 1.40(s, 3H), 1.31 (s, 3H), 0.81 (s, 3H).

1-amino-2-*t*-butoxycarbonylethane-1-boronate pinanediol ester•HCl. 1-azido-2-*t*-butoxycarbonylethane-1-boronate pinanediol ester (50 mg, 0.29 mmol) was dissolved in methanol (100 ml) and hydrogen chloride (4 N solution in dioxane) (0.040 ml, 0.32 mmol) and 10 % palladium on carbon were added. The azide was hydrogenated at 55 psi for 2 hours. The catalyst was removed by filtration and solvent was evaporated. Cold hexanes were added to give a solid. It was dried under high vacuum to give the final product (0.080 g, 0.23 mmol, 79.%). ^{1}H NMR ($CDCl_3$) δ 4.25 (t, 1H), 3.05 (t, 1H), 2.78 (m, 2H), 2.4-1.85 (m, 6H), 1.42-1.25 (2s, 12H), 0.82 (s, 3H). Analysis calculated for $C_{17}H_{30}O_4NB$ + H: 324.3. Found: 324.3.

Example 5h

Preparation of H-boroGlu(OMe)-$C_{10}H_{16}$

1-Phenylthio-3-methoxycarbonylpropane-1-boronate pinacol ester. *n*-Butyllithium (8.0 ml, 20 mmol, 2.5 M in hexanes) was added dropwise to a solution of diisopropylamine (2.91 ml, 21.0 mmol) in THF (10 ml) and stirred at 0°C in a 50 ml round bottom flask.. A solution of phenylthiomethane boronate pinacol ester (from Example 4, 5.0 g, 20.0 mmol) in THF (10 ml) was added dropwise

yielding a white precipitate. The reaction mixture was stirred for 1 hour at 0°C, followed by the dropwise addition of methyl acrylate (Aldrich) (1.80 ml, 20.0 mmol). The precipitate dissolved and the solution was allowed to warm to room temperature and stirred for 16 hours. The mixture was then treated with excess cold 10 % phosphoric acid and stirred for 5 minutes. The product was extracted into ether (100 ml). The organic layer was dried over sodium sulfate and filtered. Solvent was evaporated and the residue purified by silica gel chromatography using 10 % ethyl acetate: hexanes as a solvent to yield a clear colorless oil (0.67 g, 1.99 mmol, 10.0 %). ^{1}H NMR ($CDCl_3$) δ 7.43-7.19 (m, 5H), 3.62 (s, 3H), 2.80 (t, 1H), 2.58 (m, 2H), 1.98 (m, 2H), 1.20 (s, 12H).

1-Iodo-3-methoxycarbonyl-propane-1-boronate pinacol ester. 1-Phenylthio-3-methoxycarbonylpropane-1-boronate pinacol ester (0.45 g, 1.33 mmol) was dissolved in anhydrous acetonitrile (10 ml). Dry methyl iodide (1.70 ml, 26.6 mmol) was added, followed by the addition of sodium iodide (0.40 g, 2.66 mmol). The reaction mixture was refluxed for 8 hours. After evaporating solvent, the reaction mixture was dissolved in ether (20 ml) and was washed with water (20 ml). After drying over $MgSO_4$ and evaporating solvent, the crude product was purified by silica gel chromatography using 20 % ethyl acetate: hexanes to yield a brown oil (0.10 g, 0.28 mmol, 21 %). ^{1}H NMR ($CDCl_3$) δ 3.63 (s, 3H), 3.30 (t, 1H), 2.40 (m, 2H), 2.15 (m, 2H), 1.24 (s, 12H).

1-Azido-3-methoxycarbonylpropane-1-boronate pinacol ester . To a solution of 1-iodo-3-methoxycarbonylpropane-1-boronate pinacol ester (0.10 g, 0.28 mmol) dissolved in N,N-dimethylformamide (1 ml) was added a solution of sodium azide (0.037g, 0.56 mmol) The reaction mixture was heated at 68°C for 3 hours. The solvent was evaporated *in vacuo*.

The residue was dissolved in ethyl acetate and was washed with water (2 x 3 ml). It was dried over $MgSO_4$ and evaporated to give a brown oil. ^1H NMR ($CDCl_3$) δ 3.63 (s, 3H), 3.20 (t, 1H), 2.58 (m, 1H), 1.98 (m, 2H), 1.27 (s, 12H).

1-Azido-3-methoxycarbonylpropane-1-boronate pinanediol ester. The pinacol ester (0.42 g, 1.56 mmol) was dissolved in ether (5 ml) and pinanediol (0.29 g, 1.72 mmol) was added. The reaction was stirred for 2 hours. Purified by silica gel chromatography using 80 % hexanes: ethyl acetate gave the desired product as a light brown oil (0.13 g, 0.41 mmol, 26 %). TLC using hexanes: ethyl acetate (8:2) indicated a single spot, R_F of 0.37. ^1H NMR ($CDCl_3$) δ 4.20 (dd, 1H), 3.61 (s, 1H), 3.21(m, 1H), 2.51-1.82 (m, 10H), 1.43 (s, 3H), 1.32(s, 3H), 0.81 (s, 3H).

1-Amino-3-methoxycarbonylpropane-1-boronate pinanediol•HCl. The azide (0.078 g, 0.24 mmol) was dissolved in methanol (4 ml). Hydrogen chloride (4 N in dioxane 0.0060 ml, 0.24 mmol) and 10 % palladium on carbon were added and mixture was hydrogenated at atmospheric pressure for 2 hours. After removing the catalyst and evaporation of solvent, the residue was dried under high vacuum to give the desired product (0.040 g, 0.13 mmol, 55%). ^1H NMR ($CDCl_3$) δ 4.25 (d, 1H), 3.11 (m, 1H), 2.61-1.85 (m, 10H), 1.42 (s, 3H), 1.32 (s, 3H), 0.82 (s, 3H). Analysis calculated for $C_{15}H_{26}O_4NB$ + H: 296.4. Found: 296.4.

Example 6

Preparation of Boc-Pro-borocyclopropylmethylglycine pinanediol (Boc-Pro-NH-CH[-CH_2-cyclopropyl]$BO_2C_{10}H_{16}$)

Boc-Pro-boroAlg pinanediol ester. Boc-Proline (1.07 g, 4.95 mmol) was dissolved in THF (15 mL) and N-methylmorpholine (0.540 mL, 4.95 mmol) was added. The solution was cooled to -20°C and isobutyl chloroformate (0.640 mL, 4.95 mmol) was added. After 5 min, a cold (-20°C) solution of H-boroAlg-pinanediol•HCl (Example 1, 1.4 g, 4.95 mmol) dissolved in $CHCl_3$ (10 mL) was added followed by the addition of triethylamine (0.68 mL, 4.95 mmol). The reaction was allowed to warm to room temperature and stirred overnight. The mixture was filtered and the filtrate was concentrated *in vacuo*. After dissolving the oily residue in ethyl acetate (30 mL), it was washed with 0.2 N HCl, 5 % $NaHCO_3$ and saturated aqueous NaCl. The organic layer was dried over Na_2SO_4 and concentrated. The crude material was purified on silica gel. The column was eluted using a stepwise gradient of ethyl acetate: hexane from a ratio of 9:1 to a ratio of 1:1. TLC in 1:1 ethyl acetate / hexane indicated the product at R_F of 0.30. Fractions containing the product were concentrated *in vacuo* to give 1.1 g (50 %) of **9**. ^{1}H-NMR ($CDCl_3$) δ 5.7 - 5.9 (m, 1H), 5.03 (m, 2H), 4.25 (d,1H), 3.2 (m, 4H), 3.0 (m, 1H), 2.4 - 1.78 (m, 10H), 1.45 (s, 9H), 1.38 (s, 3H), 1.26 (s, 3H), 0.84 (s, 3H). ESI/MS calculated for $C_{24}H_{39}N_2O_5B_1$ +H: 447.4. Found: 447.4.

Boc-Pro-boroCpa pinanediol ester. Diazomethane was prepared from Diazald (Aldrich) using the procedure provided by the manufacturer. The allyl boronic acid ester (1.00 g, 2.20 mmol) was dissolved in ether (10 mL) and diazomethane (700 mg, 16.6 mmol) was added. Palladium acetate (50 mg) dissolved in THF (1 mL) was added to the flask. Vigorous bubbling was observed. The reaction was allowed to stir for 10 minutes and excess diazomethane was removed by evaporation using a stream of nitrogen. Ether was added and the reaction mixture was filtered using a paper filter. The filtrate was washed with water and saturated aqueous sodium chloride. It was dried over

anhydrous Na_2SO_4 and filtered. The filtrate was concentrated *in vacuo*. The residue was purified by silica gel chromatography by eluting with ethyl acetate: hexane (3: 7). TLC with ethyl acetate followed by a 10 min incubation in HCl chamber and ninhydrin spray indicated the product at R_F 0.58. Fractions containing product were pooled, concentrated, and dried under high vacuum to give 300 mg (29 %) of the cyclopropyl analog as white solid. ^{1}H-NMR ($CDCl_3$) δ 4.23 (dd, 1H), 3.2 - 3.0 (m, 5H), 2.31 - 1.41 (m, 10H), 1.4 (s, 9H), 1.38 (s, 3H), 1.22 (s, 3H), 0.78 (s, 3H), 0.61 (m, 2H), 0.33 (m, 2H), 0.10 (m, 1H). ESI/MS calculated for $C_{25}H_{41}N_2O_5B_1$ +H: 460.5. Found 460.5.

Example 7

Preparation of Boc-Asp(O^{t}Bu)-Glu(O^{t}Bu)-Val-Val-Pro-boroCpa pinanediol ester

H-Pro-boroCpa pinanediol ester•hydrochloride. The free N-terminal amine was prepared by treating Boc-Pro-boroCpa pinanediol ester (Example 6, 210 mg, 0.45 mmol) with 4 N HCl in dioxane (10 mL) for 2 hours. The material was concentrated *in vacuo* and dried under high vacuum to give a brown oil (180 mg, 98%). ^{1}H-NMR ($CDCl_3$) δ 4.32 (d, 1H), 3.42 (m, 4H), 1.51-2.41 (m, 10H), 1.39 (s, 3H), 1.25 (s, 3H), 0.82 (m, 5H), 0.41 (m, 2H), 0.11 (m, 2H). ESI/MS calculated for $C_{20}H_{34}N_2O_3B_1$ +H: 395.5. Found 395.5.

Boc-Asp(O^{t}Bu)-Glu(O^{t}Bu)-Val-Val-OH. Boc-Val-Val-OBzl was prepared by coupling Boc-Val-OH to H-Val-OBzl. H-Val-OBzl• HCl (5.0 g, 20.5 mmol), Boc-Val-OH (4.45 g, 20.5 mmol), and 1-hydroxybenzotriazole•H_2O (HOBT, 5.55 g, 41.1 mmol) were dissolved in 50 mL of chloroform. N-Methylmorpholine (NMM, 2.24 mL, 20.5 mmol) and N, N'-dicyclohexylcarbodiimide (DCC, 4.2 g, 20.5 mmol) were added and the reaction mixture was allowed to stir overnight at room temperature. The reaction mixture was filtered and solvent was evaporated.

Ethyl acetate was added and the mixture was filtered. The filtrate was washed with 0.20 N HCl, 5% NaHCO3, and saturated aqueous NaCl. It was dried over Na_2SO_4, filtered, and evaporated to give 7.2 g (88%) of the desired product. ^1H NMR ($CDCl_3$) δ 7.38 (s, 5H), 6.40 (d, 1H), 5.21-5.05 (m, 3H), 4.58 (m, 1H), 3.90 (t, 1H), 2.21 (m, 2H), 1.14 (s, 9H), 0.92 (m, 12H). Boc-Val-Val-OBzl (7.2 g, 17.7 mmol) was allowed to stir with 25 mL of 4N HCl: dioxane for 2 h. After removing solvent by evaporation, the residue was triturated with hexane and isolated by filtration to give 6.3 g of the amine hydrochloride. [^1H NMR ($CDCl_3$) δ 8.61 (d, 1H), 7.31 (s, 5H), 4.21 (t, 1H), 3.65 (m, 1H), 2.15 (m, 2H), 0.84 (m, 12H).]

H-Val-Val-OBzl•HCl (21.3 g, 62.1 mmol) was dissolved in 150 mL of DMF and Z-Glu(O^{t}Bu)-OH (20.9 g, 62.1 mmol), HOBT (16.8 g, 124 mmol), NMM (6.8 mL, 62.1 mmol) and DCC (12.8 g, 62.1 mmol) were added. The reaction mixture was stirred overnight at room temperature. The mixture was filtered and solvent was evaporated. Ethyl acetate was added and insoluble material was removed by filtration. The filtrate was washed with 0.2 N HCl, 5% $NaHCO_3$, and saturated aqueous NaCl. It was dried over Na_2SO_4, filtered and evaporated to give a white solid (28.2 g, 73%). ^1H-NMR ($CDCl_3$) δ 7.38 (m, 10H), 7.01 (d, 1H), 6.62 (d, 1H), 5.81 (d, 1H), 5.19 (m, 4H), 4.58 (m, 1H), 4.31 (m 2H), 2.41 - 1.82 (m, 6H), 1.41 (s, 9H), 0.98 (m, 12H).

Z-Glu(O^{t}Bu)-Val-Val-OBzl (3.0 g, 4.8 mmol) was dissolved in 150 mL methanol containing 1% acetic acid. Pearlman's catalyst, $Pd(OH)_2$, (150 mg) was added and the flask was placed on the Parr hydrogenation apparatus under an initial H_2 pressure of 50 psi. After 3 h, additional catalyst (150 mg) was added and the mixture was hydrogenated for 12 hours. The catalyst was removed by filtration through a celite pad. The filtrate was evaporated *in vacuo* to give

H-Glu(OBzl)-Val-Val-OH (1.64 g, 85.4%). ^{1}H-NMR (CD_3OD) δ 4.38 (m, 2H), 3.90 (t, 1H), 2.38 - 1.60 (, 6H), 1.41 (s, 9H), 1.00 (m, 12H).

Boc-Asp(O^{t}Bu)-Glu-(O^{t}Bu)-Val-Val-OH was prepared by coupling the tripeptide to the active ester of Boc-Asp(OBzl)-OH. Boc-Asp(O^{t}Bu)-N-hydroxysuccinimide ester was prepared by dissolving Boc-Asp(O^{t}Bu)-OH (3.00 g, 10.4 mmol) and N-hydroxysuccinimide (1.19 g, 10.4 mmol) in 50 mL of ethylene glycol dimethyl ether. The flask was cooled to 0°C in an ice bath and DCC was added. The reaction mixture stirred overnight and was allowed to warm to room temperature. The mixture was filtered and the filtrate was evaporated *in vacuo*. The residue was dissolved in ethyl acetate and refiltered. The filtrate was evaporated give a white solid. Recrystallized from ethyl acetate: hexane gave the N-hydroxysuccinimide ester (3.38g, 84%). ESI/MS calculated for $C_{17}H_{26}N_2O_8$ +H: 387.2. Found: 387.4. Boc-Asp(O^{t}Bu)-N-hydroxysuccinimide ester (4.37 g, 11.3 mmol) was dissolved in 100 mL of dioxane and was added to a solution of H- Glu-(O^{t}Bu)-Val-Val-OH (4.92 g, 12.3 mmol) dissolved in 150 mL of water and 50 mL of dioxane. Sodium bicarbonate (3.07 g, 36.7 mmol) was added and the mixture was stirred at room temperature for 5 h. Dioxane was removed *in vacuo* and concentrated HCl was added to adjust the pH to approximately 2. The product was extracted into ethyl acetate. The ethyl acetate solution was washed with 0.2 M HCl and saturated NaCl. It was dried over sodium sulfate, filtered, and evaporated to yield the protected tetrapeptide as a white solid (7.5 g, 90.6 %). ^{1}H-NMR ($CDCl_3$) δ 7.58 - 7.41 (m, 3H), 5.78 (d, 1H), 4.57 (m, 4H), 2.78 - 1.83 (m, 8H), 1.40 (3s, 27H), 0.98 (m, 12H). ESI/MS calculated for $C_{32}H_{56}N_4O_{11}$: +H: 673.5. Found: 673.5.

Boc-Asp(O^{t}Bu)-Glu(O^{t}Bu)-Val-Val-Pro-boroCpa-pinanediol was prepared by coupling the protected tetrapeptide to the dipeptidyl boronic acid. H-Pro-boroCpa pinanediol ester•

HCl (180 mg, 0.46 mmol) and Boc-Asp(O^tBu)-Glu(O^tBu)-Val-Val-OH (310 mg, 0.46 mmol) were dissolved in chloroform (15 mL) and HOBT (120 mg, 0.92 mmol) and NMM (50 µL, 0.46 mmol) were added. The reaction mixture was gently heated until dissolution. DCC (95 mg, 0.46 mmol) was added and a white precipitate was seen within 10 minutes. The reaction was allowed to stir for 24 hours. The reaction mixture was filtered through celite and the filtrate was concentrated *in vacuo*. The oily residue was dissolved in ethyl acetate and additional solids were removed by filtration. The filtrate was washed with 0.20 N HCl (30 mL), 5% $NaHCO_3$ (30 mL), and saturated aqueous NaCl (30 mL). The organic phase was dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. The crude product was purified by silica gel chromatography using a stepwise gradient from ethyl acetate: hexane (2: 8) to ethyl acetate: hexane (4: 6). TLC in ethyl acetate indicated the compound had an R_F of 0.37. Fractions containing product (R_F. 0.37 by TLC in ethyl acetate) were pooled and evaporated to give 110 mg (23%) of the desired product as a white solid. ^{1}H-NMR ($CDCl_3$) δ 7.02 (d, 1H), 5.60 (d, 1H), 4.9 - 4.20 (m, 6H), 4.23 (dd, 1H), 3.58 - 3.81 (m, 4H), 2.95 (m, 1H), 2.41 - 1.81 (m, 16H), 1.41 (3s, 27 H), 1.36 (s, 3H), 1.21 (s, 3H), 1.1 - 0.81 (m, 15H), 0.62 (m, 2H), 0.39 (m, 2H), 0.10 (m, 1H). ESI/MS calculated for $C_{52}H_{87}N_6O_{13}B_1$ +H: 1016.1. Found 1016.1.

Example 8

H-Asp-Glu-Val-Val-Pro-boroCpa pinanediol ester•HCl

The protected peptide, Example 7, (26 mg, 0.025 mmol) was treated with 4 N HCl in dioxane (10 mL) for 2 hours. The solution was evaporated *in vacuo* and dried under high vacuum to give 16 mg (76 %) of the desired product as a yellow solid. ^{1}H-NMR (CD_3OD) δ 8.0 (d, 1H), 4.51-4.11 (m, 5H), 3.1-2.75 (m, 4H), 2.40 (m, 4H), 2.38-1.80 (m, 16H), 1.38 (s, 3H), 1.36 (s, 3H), 1.10-0.82 (m, 17H), 0.41 (m,

2H), 0.11 (m, 1H). ESI/MS calculated for $C_{39}H_{63}N_6O_{11}B_1$ +H: 801.5. Found 801.5.

Example 9

Preparation of Boc-Asp(O^tBu)-Glu(O^tBu)-Val-Val-Pro-boroAlg-pinanediol.

Preparation of Boc-Asp(O^tBu)-Glu(O^tBu)-Val-Val-Pro-OH.

Boc-Val-Pro-OBzl was prepared by dissolving H-Pro-OBzl (20 g, 83 mmol) in 50 mL of chloroform and adding Boc-Val-OH (18.0 g, 83 mmol), HOBt (23.0g, 165 mmol), NMM (9.0 mL, 83 mmol) and DCC (17.0 g, 83 mmol). The reaction mixture was stirred overnight at room temperature. The mixture was filtered and solvent was evaporated. Ethyl acetate was added and insoluble material was removed by filtration. The filtrate was washed with 0.2N HCl, 5% $NaHCO_3$, and saturated aqueous NaCl. It was dried over Na_2SO_4, filtered and evaporate to give a white solid (30 g, 75 mmol, 90%). ESI/MS calculated for $C_{22}H_{32}N_2O_5$ +H: 405.2. Found 405.6.

Boc-Val-Val-Pro-OBzl was prepared by dissolving Boc-Val-Pro-OBzl (14.0 g, 35.0 mmol) in 4N HCl in dioxane (20 mL) and allowing the reaction to stir for 2 h under an inert atmosphere at room temperature. The reaction mixture was concentrated by evaporation *in vacuo* and ether was added to yield a precipitate. It was collected by filtration under nitrogen. After drying *in vacuo* with P_2O_5, H-Val-Pro-OBzl was obtained as a white solid (22.6 g, 30.3 mmol, 89%). (ESI/MS calculated for $C_{17}H_{24}N_2O_3$ +H: 305.2. Found: 305.2.) H-Val-Pro-OBzl (9.2 g, 27 mmol) was dissolved in 50 mL of CH_2Cl_2 and Boc-Val-OH (7.3 g, 27 mmol), HOBt (7.3 g, 54 mmol), NMM (3.0 mL, 27 mmol) and DCC (5.6 g, 27 mmol) were added. The reaction mixture stirred overnight at room temperature. The mixture was filtered and the filtrate was evaporated. The residue was dissolved in ethyl acetate and the solution was re-filtered. The filtrate was washed with 0.2N HCl, 5% $NaHCO_3$, and saturated aqueous NaCl. It was

dried over Na_2SO_4, filtered and evaporated to give a yellow oil (10.6 g, 21.1 mmol, 78%). ESI/MS calculated for $C_{27}H_{41}N_3O_6$ + Na: 526.3 Found: 526.4.

Z-Glu(O^{t}Bu)-Val-Val-Pro-OBzl was also prepared by DCC coupling. H-Val-Val-Pro-OBzl•hydrochloride was obtained in a 100% yield by treating the corresponding Boc compound with anhydrous HCl using the procedure described for H-Val-Pro-OBzl (ESI/MS calculated for $C_{22}H_{33}N_3O_4$ + H: 404.2. Found 404.3.). The amine hydrochloride (7.40 g, 16.8 mmol) was dissolved in 185 mL DMF and 25 mL THF. Z-Glu(O^{t}Bu)-OH (5.60 g, 16.8 mmol), HOBt (4.60 g, 33.6 mmol), NMM (1.85 mL, 16.8 mmol) and DCC (3.5 g, 16.8 mmol) were added. The reaction was run and the product was isolated by the procedure described for Boc-Val-Val-Pro-OBzl. The tetrapeptide was obtained as a white foam (12.0 g, 16.1 mmol, 96%). ESI/MS calculated for $C_{39}H_{54}N_4O_9$ + Na: 745.4. Found: 745.4.

H-Glu(O^{t}Bu)-Val-Val-Pro-OH was prepared by dissolving Z-Glu(O^{t}Bu)-Val-Val-Pro-OBzl (2.90 g, 3.89 mmol) in 100 mL methanol containing 1% acetic acid. Pearlman's catalyst, $Pd(OH)_2$, (100mg) was added and the flask was placed on the Parr hydrogenation apparatus with an initial H_2 pressure of 34 psi. After three hours, the catalyst was removed by filtration through a celite pad and the filtrate was evaporated *in vacuo* to yield a yellow oil (1.30 g, 2.61 mmol, 67%). ESI/MS calculated for $C_{24}H_{42}N_4O_7$ +H: 499.3 Found: 499.4.

Boc-Asp(O^{t}Bu)-Glu(O^{t}Bu)-Val-Val-Pro-OH was prepared by active ester coupling. Boc-Asp(O^{t}Bu)-N-hydroxysuccinimide ester was prepared by coupling Boc-Asp(OtBu)-OH (3.00 g, 10.4 mmol) to N-hydroxysuccinimide (1.19 g, 10.4 mmol) in 50 mL of ethylene glycol dimethyl ether. The reaction flask was placed in an ice bath at 0°C and DCC was added. The reaction mixture was slowly allowed to warm to room

temperature and to stir overnight. The mixture was filtered and the filtrate was evaporated *in vacuo*. The residue was dissolved in ethyl acetate and re-filtered. The filtrate was evaporated give a white solid. Recrystallized from ethyl acetate: hexane gave the activated ester (3.38 g, 8.80 mmol, 84%). (ESI/MS calculated for $C_{17}H_{26}N_2O_8$ + H: 387.2. Found: 387.4.) H-Glu(O^tBu)-Val-Val-Pro-OH (5.40 g, 10.8 mmol) was dissolved in 100 mL of water. Sodium bicarbonate (0.92 g, 11.0 mmol) was added followed by triethylamine (2.30 mL, 16.5 mmol). The N-hydroxysuccinimide ester (3.84 g, 10.0 mmol) was dissolved in 100 mL dioxane and was added to the H-Glu(O^tBu)-Val-Val-Pro-OH solution. The mixture stirred overnight at room temperature. Dioxane was removed *in vacuo* and 1.0 M HCl was added to give pH ~ 1. The product was extracted into ethyl acetate. The ethyl acetate solution was washed with 0.2 N HCl, dried over sodium sulfate, filtered, and evaporated to yield a yellow oil (7.7 g, 10.0 mmol, 100%). ESI/MS calculated for $C_{37}H_{63}N_5O_{12}$ + Na: 792.4. Found: 792.4.

Boc-Asp(O^tBu)-Glu(O^tBu)-Val-Val-Pro-boroAlg-pinanediol was prepared by coupling the protected pentapeptide to H-boroAlg-pinanediol (Example 1). Boc-Asp(O^tBu)-Glu(O^tBu)-Val-Val-Pro-OH (1.8 g, 2.3 mmol) was dissolved 10 mL THF and was cooled to -20°C. Isobutyl chloroformate (0.30 mL, 2.3 mmol) and NMM (0.25 mL, 2.3 mmol) were added. After 5 minutes, this mixture was added to **4** (0.67 g, 2.3 mmol) dissolved in THF (8 mL) at -20°C. Cold THF (~5 mL) was used to aid in the transfer. Triethylamine (0.32 mL, 2.3 mmol) was added and the reaction mixture was allowed to come to room temperature and to stir overnight. The mixture was filtered and solvent was removed by evaporation. The residue was dissolved in ethyl acetate, washed with 0.2 N HCl, 5% $NaHCO_3$, and saturated NaCl. The organic phase was dried with Na_2SO_4, filtered, and evaporated to yield a yellow oil. Half of the crude

product (1.5 g) was purified in 250 mg lots by HPLC using a 4 cm x 30 cm Rainin C-18 reverse phase column. A gradient from 60: 40 acetonitrile: water to 100% acetonitrile was run over a period of 28 minutes at a flow rate of 40 mL/min. The fractions containing the desired product were pooled and lyophilized to yield a white solid (46 mg). ^{1}H-NMR (CD_3OD) δ 0.9-1.0 (m, 15H), 1.28 (s, 3H), 1.3 (s,3H), 1.44 (3s, 27H), 1.6-2.8 (20H), 3.7(m,1H), 3.9(m, 1H), 4.1-4.7 (7H), 5.05(m, 2H), 5.9(m, 1H). High res (ESI/MS) calculated for $C_{51}H_{86}N_6O_{13}B_1$ +H: 1001.635. Found 1001.633.

Example 10

Preparation of H-Asp-Glu-Val-Val-Pro-boroAlg pinanediol ester•trifluoroacetate .

The hexapeptide analog, Example 9, (22.5 mg, 0.023 mmol) was treated with 2 mL of TFA: CH_2Cl_2 (1: 1) for 2 h. The material was concentrated *in vacuo* and purified by HPLC using C-18 Vydac reverse phase (2.2 x 25 cm) column with a gradient starting at 60:40 acetonitrile/water with 0.1%TFA going to 95:5 over 25 minutes with a flow rate of 8 mL/min. The product eluted at 80% acetonitrile. The fractions were evaporated and dried under high vacuum to give 8.9 mg (49%) of the desired product as white amorphous solid. ^{1}H-NMR (CD_3OD) δ 5.82 (m, 1H), 5.02 (m, 2H), 4.58(m, 1H), 4.42 (m, 3H), 4.18 (m, 4H), 3.90 (m, 1H), 3.62 (m, 1H), 3.01 (dd, 1H), 2.78 (m, 1H), 2.62 (m, 1H), 2.41-1.78 (m, 17H), 1.31 (s, 3H), 1.28 (s, 3H), 1.10 - 0.82 (m, 15H). ESI/MS calculated for $C_{38}H_{62}N_6O_{11}B$ +H: 789.2. Found: 789.2.

Example 11

Preparation of Ac-Asp(O^{t}Bu)-Glu(O^{t}Bu)-Val-Val-Pro-boroAlg-$C_{10}H_{16}$.

Ac-Asp(O^{t}Bu)-Glu(O^{t}Bu)-Val-Val-Pro-OH was prepared by coupling the N-hydroxysuccinimde ester of Ac-Asp(OBzl)-OH to H-Glu(OtBu)-Val-Val-Pro-OH (See Example 9.) The

tetrapeptide (2.67 g, 5.36 mmol) was dissolved in 100 mL of water and $NaHCO_3$ (0.45g, 5.36 mmol) and triethylamine (1.12 mL, 8.00 mmol) were added. Ac-Asp(OtBu)-N-hydroxysuccinimide (1.58 g, 4.8 mmol) was dissolved in 100 mL of dioxane and added. After stirring overnight, most of the dioxane was removed by evaporation and the remaining aqueous solutions was acidified with HCl. The product was extracted into ethyl acetate and was washed with 0.10 N HCl and with saturated aqueous NaCl prepared in 0.10 N HCl. It was dried over anhydrous Na_2SO_4, filtered, and evaporated to yield 1.85 g of crude product. A final product (1.5 g, 40% yield) was obtained by crystallization from ethyl acetate and washing with ether.

Ac-Asp(O^tBu)-Glu(O^tBu)-Val-Val-Pro-OH (1.53 g, 2.15 mmol) was dissolved in 7 mL of DMF and NMM (0.23 mL, 2.15 mmol) was added. The solution was cooled to -20°C and isobutyl chloroformate (0.28 mL, 2.15 mmol) was added. After 5 min, H-boroAlg-$C_{10}H_{16}$•HCl (0.59 g, 2.15 mmol) dissolved in 10 mL of cold THF and triethylamine (0.300 mL, 2.15 mmol) were added. The reaction mixture was allowed to come to room temperature and to stir overnight. The reaction mixture was filtered and the filtrate evaporated. The residue was dissolved in ethyl acetate and was washed with 5% $NaHCO_3$, 0.20 N HCl, and saturated aqueous NaCl. After drying over Na_2SO_4, filtering, and evaporating solvent, the residue was purified by chromatography on silica gel using ethyl acetate as a solvent to yield 1.85 g of the desired product. Anal. Calcd. for $C_{48}H_{78}N_6O_{12}B$ - H: 941.6. Found: 941.6.

Example 12

Preparation of Ac-Asp-Glu-Val-Val-Val-Pro-boroAlg-$C_{10}H_{16}$.

Ac-Asp(O^tBu)-Glu(O^tBu)-Val-Val-Pro-boroAlg-$C_{10}H_{16}$, Example 11, (0.50 g, 0.53 mmol) was dissolved in 3 mL of 4 N HCl in dioxane and was allowed to stir 2 h. Solvent was removed

by evaporation and the residue was triturated with ether and dried under high vacuum to give 0.40 g (90%) of product. Anal. Calcd. for $C_{40}H_{62}N_6O_{12}B$ + H: 830.78: Found: 831.1.

Example 13

Preparation of Ac-Asp(OMe)-Glu(OMe)-Val-Val-Val-Pro-boroAlg-$C_{10}H_{16}$.

Ac-Asp-Glu-Val-Val-Val-Pro-boroAlg-$C_{10}H_{16}$, Example 12, (50 mg) was dissolved in 2 mL of methanol and 5 mL of diazomethane: ether were added. After ~30 min solvent and excess diazomethane were removed by evaporation under a stream of nitrogen to yield 47 mg of the desired product. Anal. Calcd for $C_{42}H_{67}BN_6O_{12}$ + H: 859.8. Found: 859.6.

Example 14

Preparation of Ac-Asp-Glu-Val-Val-Pro-boroAlg-OH.

Ac-Asp-Glu-Val-Val-Val-Pro-boroAlg-$C_{10}H_{16}$, Example 12, (50 mg, 0.060 mmol) was dissolved in 20 mL of 50 mM ammonium acetate; 20 mL of ether and phenyl boronic acid (37 mg, 0.30 mmol) were added. The mixture was stirred for 7 h. Phases were separated and the ether phase was washed with 2 mL of water. The combined aqueous phases were washed with two 20 mL portions of ether and were lyophilized. The residue was dissolved in water and was chromatogramed on a 2 X 20 cm column containing BioRad™ P2 resin to yield 25 mg of the desired free boronic acid peptide. Anal. Calcd. for [($C_{30}H_{49}BN_6O_{12}$) - 2H]/2: 347.2. Found: 347.3.

Example 15

Preparation of Boc-Asp(O^tBu)-Glu(O^tBu)-Val-Val-Pro-boroVinylgly-Pinanediol Ester.

Boc-Asp(O^tBu)-Glu(O^tBu)-Val-Val-Pro-OH (See Example 9) (1.51 g, 1.95 mmol) was dissolved in THF (20 mL) and cooled

to -20°C. Isobutylchloroformate (0.251 mL, 1.95 mmol) and 4-methylmorpholine (0.214 mL, 1.95 mmol) were added. After 5 min, a solution of boroVinylglycine pinanediol ester, Example 5, (0.529 g, 1.95 mmol) dissolved in DMF (20 mL) and cooled to -20°C was added. Triethylamine (0.272 mL, 1.95 mmol) was added and the resulting solution was allowed to stir for an additional 20 h while warming to room temperature. The solution was then filtered and the solvent removed *in vacuo*. The residue was dissolved in ethyl acetate (100 mL), washed with 0.2 N HCl (100 mL), 5% NaHCO3 (100 mL), brine (100 mL), dried with Na_2SO_4, filtered and concentrated *in vacuo* to yield a pale orange residue. This was purified first by LH-20 chromatography using 2.5 x 90 cm column and methanol as a solvent. Final purification was achieved by preparative HPLC on 180 mg aliquots using a 4 cm x 30 cm Rainin C18 reverse phase column. A gradient from 60:40, acetonitrile: water to 100% acetonitrile was ran over 28 min at flow rate of 40 mL/min, to yield 188 mg of the desired product as a white solid (0.19 mmol, 9.8% yield). ESI/MS Calculated for $C_{50}H_{84}N_6O_{13}B_1$+ H: 988.6. Found: 988.7. ^{1}H-NMR (CD_3OD) d 0.85 (s, 3H), 0.91 (t, 6H), 0.99 (t, 6H) 1.26 (s, 3H) 1.29 (s, 3H) 1.44 (s, 27H), 1.6-2.4 (m, 15 H), 2.57 (dd, 1H), 2.87 (dd, 1H), 3.26 (d, 1H), 3.77 (m, 1H), 3.96 (m, 1H), 4.10 (m, 2H), 4.39 (m, 4H), 4.61 (m, 2H), 4.85-5.05 (m, 2H), 5.82 (m, 1H).

Example 16

Boc-Asp(O^{t}Bu)-Glu(O^{t}Bu)-Val-Val-Pro-boroCyclopropylglycine-pinanediol ester

Boc-Asp(OtBu)-Glu(OtBu)-Val-Val-Pro-OH (See Example 9.) (1.5 g, 1.9 mmol) was dissolved in THF (15 mL) and N-methylmorpholine (0.21 mL, 1.9 mmol) was added. The solution was cooled to -20°C and isobutylchloroformate (0.25 mL, 1.9 mmol) was added. This solution was stirred for 10 min and a -20°C solution of the cyclopropyl boronic

acid pinacol ester, Example 3, (0.46g, 1.9 mmol) in THF (15 mL) was added followed quickly by triethylamine (0.27 mL, 1.9 mmol). The resulting mixture was stirred at -20°C for 1 h and then allowed to warm to room temperature and stir for 2 h. (+)-Pinanediol (0.66 g, 3.9 mmol) was added and the solution was stirred for 16 h. The solution was concentrated and re-dissolved in ethyl acetate, washed with 0.20 N HCl (2 x 100 mL), 5% $NaHCO_3$ (2 x 100 mL), saturated aqueous NaCl, dried over anhydrous Na_2SO_4 and concentrated to yield a white foam. This was purified on a 2.5 x 42 cm column of Sephadex™ LH-20 in methanol. Fractions 9-15 were collected (10 mL/fraction). This material, in 120 mg portions, was further purified by preparative HPLC using a 4 x 30 cm Rainin C-18 reverse phase column. A gradient from 40: 60 acetonitrile: water to 100% acetonitrile was run over a period of 45 min at a flow rate of 40 mL/min. The fractions eluting at 27 min were combined to yield a white solid (97 mg, 4.9% yield). ^1H NMR d 0.17 (m, 2H), 0.48 (d, 3H), 0.87-1.01 (m, 16H), 1.28 (s, 3H), 1.31 (s, 3H), 1.44 (s, 27H), 1.55-2.33 (m, 18H), 2.65 (ddd, 2H), 3.63 (m, 2H), 3.94 (m, 2H) 4.1-4.7 (m, 8H); ESI *m/z* calculated for $C_{51}H_{85}BN_6O_{13}Na$: 1023.6 Found: 1023.7.

Example 17

H-Asp-Glu-Val-Val-Pro-boroCyclopropylglycine-pinanediol ester•HCl

The protected peptide, Example 16, (62 mg, 0.06 mmol) was allowed to react with 4 N HCl in dioxane (5 mL) at room temperature under nitrogen for 3.5 h. The solvent was removed by evaporation to give a white amorphous powder. After drying under high vacuum with P_2O_5 and KOH, 32.5 mg of the desired product was obtained in a 65% yield. ESI *m/z* calculated for $C_{38}H_{61}BN_6O_{11}Na$: 811.4. Found: 811.5. ^1H NMR (CD_3OD d 0.10 (m, 2H), 0.86 (m, 3H), 0.87-1.14 (m, 17H), 1.28 (s, 3H), 1.32 (s, 3H), 1.75-2.40 (m, 8H), 2.80

(dd, 1H), 3.01 (m, 2H), 3.70 (m, 2H), 3.93 (m, 1H), 4.15-4.22 (m, 1H), 4.45 (m, 1H), 4.54 (m, 1H).

Example 18

Preparation of Pz-CO-Val-Val-Hyp(OBzl)-boroAbu-pinanediol.

H-Hyp(Bzl)-boroAbu-pinanediol. The mixed anhydride of Boc-Hyp(OBzl)-OH (2.48 g, 7.71 mmol) was prepared and coupled H-boroAbu-$C_{10}H_{16}$ (Example 2) by the procedure described for the preparation of Example 6. The final product was purified by silica gel chromatography using ethyl acetate: hexane as a solvent. Boc-Hyp(OBzl)-boroAbu-pinanediol was obtained in a yield of 55%. ^{1}H NMR ($CDCl_3$) δ 7.26 (m, 5H), 6.31 (d, 1H), 4.49 (s, 2H), 4.30 (d, 1H), 3.81 (m, 1H), 3.42 (m, 2H), 3.00 (m, 1H), 2.62-1.78 (m, 7H), 1.45 (s, 9H), 1.38 (s, 3H), 1.27 (m, 5H), 0.95 (t, 3H), 0.84 (s,3H). ESI/MS calcd. for $C_{30}H_{45}BN_2O_6$ + Na: 563.4. Found: 563.4. The Boc compound (2.3 g, 4.8 mmol) was treated with 10 mL of 4 N HCl: dioxane for 2 h. After evaporating solvent and drying in vacuo H-Hyp(OBzl)-boroAbu-C10H16•HCl was obtained in a yield of 79%. ^{1}H NMR ($CDCl_3$) δ 7.38 (m, 5H), 4.58 (d, 2H), 4.41 (m, 3H), 3.51 (m, 2H), 3.05 (t, 1H), 2.41-1.60 (m, 7H), 1.39 (s, 3H), 0.97 (m, 3H), 0.87 (s, 3H).

Pz-CO-Val-Val-Hyp(Bzl)-boroAbu-pinanediol. Pz-CO-Val-Val-Hyp(OBzl)-boroAbu-pinanediol was prepared by coupling the two dipeptide analogs. The pyrazine peptide was prepared by coupling pyrazine carboxylic acid (2.14 g, 17.3 mmol) to H-Val-Val-OBzl (See Example 7.) in 50 mL of chloroform using the DCC coupling procedure described for the preparation of Example 7. Pz-CO-Val-Val-OBzl was obtained in a yield of 86%. 1H NMR ($CDCl_3$) d 9.38 (d, 1H), 8.78 (d, 1H), 8.56 (m, 1H), 8.37 (d, 1H), 7.39 (s, 5H), 6.41 (d, 1H), 5.23 (q, 2H), 4.62 (m, 1H), 4.43 (m, 1H), 2.37 (m, 2H), 1.02 (m, 6H), 0.99 (m, 6H). Pz-CO-Val-Val-OBzl (3.0 g, 7.26 mmol) was dissolved in 40 mL of dioxane and 40 mL of 1 N aqueous NaOH were added. After allowing the

solution to stir for 1 h, the pH was adjusted to 3 with HCl and dry NaCl was added to give a near saturated solution. The product was extracted into ethyl acetate. After drying over Na_2SO_4, the solution was evaporated to give 2.0 g of Pz-CO-Val-Val-OH. ^1H NMR ($CDCl_3$) d 9.24 (d, 1H), 8.81 (d, 1H), 8.75 (m, 1H), 4.42 (m, 1H), 4.35 (m, 3H), 2.23 (m, 2H), 1.18 (m, 12H).

Pz-CO-Val-Val-OH (0.58 g, 1.63 mmol) was coupled to H-Hyp(OBzl)-boroAbu-$C_{10}H_{16}$ by the DCC coupling procedure described in the preparation of Example 7. After purification by silica gel chromatography using ethyl acetate: hexane as a solvent, the desired product was obtained in a yield of 27%. ^1H NMR ($CDCl_3$) δ 9.40 (d, 1H), 8.76 (d, 1H), 8.58 (m, 1H), 8.45 (d, 1H), 7.38 (s, 5H), 4.82-4.61 (m, 3H), 4.55 (d, 2H), 4.38 (m, 1H), 4.21 (dd, 1H), 4.00 (d, 1H), 3.71 (dd, 1H), 3.03 (m, 1H), 2.41-1.82 (m, 10H), 1.36 (s, 3H), 1.28-1.24 (m, 5H), 0.95-0.82 (m, 18H). ESI/MS calcd. for $C_{40}H_{57}BN_6O_7$ + Na: 767.5. Found: 767.5.

Example 19

Preparation of Boc-Asp(O^tBu)-Glu(O^tBu)-Val-Val-Pro-boroAPe-pinanediol. (boroAPe-pinanediol is -NH-CH[-CH_2-CH_2-CH_3]BO_2-$C_{10}H_{16}$)

Boc-Asp(O^tBu)-Glu(O^tBu)-Val-Val-Pro-boroAlg-pinanediol, Example 9, (0.040 g, 0.040 mmol) was dissolved in 15 mL of methanol and the compound was hydrogenated on a Parr apparatus for 5 h in the presence of 100 mg of 10% Pd/C. Catalyst was removed by filtration and the filtrate evaporated to yield 35 mg of the desired product. ^1H NMR ($CDCl_3$) d 7.75 (m, 2H), 7.05 (d, 1H), 6.98 (d, 1H), 5.62 (d, 1H), 4.64-4.21 (m, 7H), 3.84-3.58 (m, 2H), 3.00 (m, 1H), 2.81-1.78 (m, 20H), 1.44 - 1.42 (3s, 27H), 1.40 (s, 3H), 1.25 (s, 3H), 0.98 (m, 18H). ESI/MS calcd. for $C_{51}H_{87}BN_6O_{13}$ + H: 1003.7. Found: 1003.7.

Example 20

Preparation of H-Asp-Glu-Val-Val-Pro-boroApe-pinanediol•HCl

Example 19 (0.025 g, 0.025 mmol) was treated with 2 mL of 4N HCl:dioxane for 2 h. Solvent was evaporated to yield 20 mg of the desired product. ^{1}H NMR (CD_3OD) δ 4.58-3.62 (m, 8H), 3.0 (m, 1H), 2.82-1.79 (m, 20 H), 1.34 (s, 3H), 1.22 (s , 3H). 0.95 (m, 18H). ESI/MS calcd. for $C_{38}H_{63}N_6O_{11}B$ - H: 789.6. Found: 789.6.

Example 21

Preparation of_Ac-Asp(O^tBu)-Glu(O^tBu)-DPA-Glu(O^tBu)-Cha-boroAlg pinanediol ester

Ac-Asp(O^tBu)-Glu(O^tBu)-DPA-Glu(O^tBu)-Cha-OH was prepared on Sasrin resin according to a procedure previously described (Mergler, M.; Nyfeler, R.; Tanner, R.; Gosteli, J.; Grogg, P. *Tetrah. Lett.*, **29**, 4009-4012 (1988). The peptide carboxylate (0.10 g, 0.10 mmol) was dissolved DMF (1.4 mL) and cooled to -20°C in a carbon tetrachloride/dry ice bath. Isobutyl chloroformate (13 µL, 0.10 mmol) and N-methylmorpholine (11 µL, 0.10 mmol) were added and after 5 minutes, this mixture was added to a solution consisting of H-boroAlg-$C_{10}H_{16}$•HCl, Example 1 (29.0 mg, 0.10 mmol) dissolved in DMF(0.7 mL) also chilled to -20°C. Triethylamine (14 µL, 0.10 mmol) was added. The reaction mixture was allowed to warm to room temperature and to stirred overnight. The mixture was filtered, and concentrated *in vacuo*. The residue was dissolved in ethyl acetate, washed with 0.20 N HCl, 5% $NaHCO_3$, and saturated aqueous NaCl. The product was purified by silica gel chromatography using a stepwise gradient of chloroform: methanol. Fraction containing the desired product gave a single spot, Rf 0.39, in TLC using chloroform: methanol (9:1). The desired product was obtained in a yield of 30

mg (25%). ESI/MS calculated for $C_{66}H_{97}N_6O_{14}B_1$+Na: 1231.7. Found: 1231.8.

Example 22

Ac-Asp-Glu-Dpa-Glu-Cha-boroAlg pinanediol ester

Ac-Asp(O^tBu)-Glu(O^tBu)-Dpa-Glu(O^tBu)-Cha-boroAlg$C_{10}H_{16}$, Example 21, (60 mg, 0.050 mmol) was dissolved in 1 mL 4 N HCl in dioxane and it was stirred for 1 h at room temperature. The reaction mixture was evaporated to yield an oil which was purified by HPLC using C-18 Rainin reverse phase (4 x 30 cm) column with a gradient from 60% acetonitrile: water to 100% acetonitrile. All solvent contained 0.1%TFA. The desired product eluted at 100% acetonitrile. Fractions were pooled and lyophilized to yield a white solid (10 mg). ESI/MS calculated for $C_{54}H_{73}N_6O_{14}B_1$ + Na: 1063.5. Found: 1063.6.

Example 23

Ac-Pro-boroAlg pinanediol ester

The synthesis of Boc-Pro-boroAlg-$C_{10}H_{16}$ is described in the preparation of Example 6. The Boc peptide (1.0 g, 2.2 mmol) was dissolved in 10 mL of 1:1 TFA: CH_2Cl_2 and stirred at room temperature for 1 h. Solvent was evaporated to yield H-Pro-boroAlg-$C_{10}H_{16}$•TFA (0.76 g, 91%). ESI/MS calculated for $C_{19}H_{31}N_2O_3B$ +H: 347.2. Found: 347.4. H-Pro-boroAlg-$C_{10}H_{16}$•TFA, (50 mg, 0.10 mmol) was dissolved in methylene chloride (10 mL). Acetic anhydride (8.5 µL) and diisopropylethylamine (31 µL) were added and the reaction mixture stirred at room temperature for 2 h. The mixture was washed with 0.20 N HCl, 5% $NaHCO_3$, and saturated aqueous NaCl. The organic phase was concentrated to yield a yellow oil which was further purified by HPLC using a C-18 Rainin reverse phase (4 x 30 cm) column with a gradient from 0 to 100% acetonitrile (All solvents contained 0.10%

TFA). The desired product eluted at 100% acetonitrile. Solvent was evaporated to give 5.0 mg of product. ESI/MS calculated for $C_{21}H_{33}N_2O_4B_1$ + H: 389.3. Found: 389.3.

Example 24

Preparation of Boc-Val-Pro-boroAlg-pinanediol

Boc-Val-Pro-OH was prepared by dissolving Boc-Val-Pro-OBzl, (See the preparation of Example 9, 7.80 g, 19.3 mmol) in 100 mL methanol containing 1% acetic acid. Pearlman's catalyst, $Pd(OH)_2$, (100 mg) was added and the compound was hydrogenated on a Parr apparatus. After hydrogen consumption was complete, the catalyst was removed by filtration through a celite pad and the filtrate was evaporated *in vacuo* to yield an oil (6.1 g, 100%). ESI/MS calculated for $C_{15}H_{26}N_2O_5$ +H: 315.2. Found: 315.3.

The mixed anhydride of Boc-Val-Pro-OH (1.3 g, 4.1 mmol) prepared in DMF (14 mL) by the method described for Example 6 and it was added to H-boroAlg-$C_{10}H_{16}$•HCl (1.2 g, 4.1 mmol) dissolved in DMF (9 mL). The product was purified by silica gel chromatography using a stepwise gradient of hexane: ethyl acetate. The desired product was eluted with 100% ethyl acetate. TLC in ethyl acetate indicated a single spot at R_F 0.41. Solvent was removed by evaporation *in vacuo* to yield a foam (1.27 g, 2.3 mmol, 57%). ESI/MS calculated for $C_{29}H_{48}N_3O_6B$+H: 546.4. Found: 546.3.

Example 25

H-Val-Pro-boroAlg pinanediol ester•TFA

Example 24 (100 mg, 0.18 mmol) was dissolved in 2 mL of 1:1 TFA: CH_2Cl_2 and stirred at room temperature for 2. The reaction mixture was evaporated *in vacuo* and stored under vacuum with P_2O_5 overnight to yielded a yellow solid (80 mg, 0.17 mmol, 94%). ESI/MS calculated for $C_{24}H_{40}N_3O_4B$ +H: 446.3. Found: 446.3.

Example 26

Ac-Val-Pro-boroAlg pinanediol ester

H-Val-Pro-boroAlg-C10H16•TFA (Example 25, 50.0 mg, 0.090 mmol) was dissolved in 10 ml methylene chloride. Acetic anhydride (8.5 µL, 0.090 mmol) and diisopropylethylamine (31 µL, 0.18 mmol) were added and the reaction mixture stirred for 2 h at room temperature. The mixture was washed with 0.20 N HCl, 5%$NaHCO_3$, and saturated aqueous NaCl. The organic phase was concentrated to yield a yellow oil which was further purified by HPLC using C-18 Rainin reverse phase (4 x 30 cm) column with a gradient from 100% water to 100% acetonitrile (All solvents contained 0.1% TFA). The product eluted at 100% acetonitrile. The pooled fractions were concentrated and lyophilized to yield a white solid (5.0 mg, 0.010 mmol, 20%). ESI/MS calculated for $C_{26}H_{42}N_3O_5B_1$ + Na: 509.4. Found: 509.3.

Example 27

Boc-Val-Val-Pro-boroAlg-pinanediol

Boc-Val-Val-Pro-OBzl, (See preparation of Example 9) (1.2 g, 2.4 mmol) was dissolved in 100 mL of methanol with 1% acetic acid. Pearlman's catalyst, $Pd(OH)_2$, (100mg) was added and the flask was placed on the Parr hydrogenation apparatus under an initial hydrogen pressure of 30 psi. After 3 h, the catalyst was removed by filtration through a celite pad. The filtrate was concentrated in vacuo to yield the carboxylic acid (0.83 g, 87%). ESI/MS calculated for $C_{20}H_{35}N_3O_6$+H: 413.3. Found: 414.2.

The mixed anhydride of Boc-Val-Val-Pro-OH (0.83 g, 2.0 mmol) was prepared in THF (10 mL) and added to H-boroAlg pinanediol ester (Example 1) dissolved in $CHCl_3$ (6 mL) using the procedure describe in Example 6. The product was purified by silica gel chromatography by first eluting the

column with a stepwise gradient of hexane: ethyl acetate and then eluting with ethyl acetate: methanol (9: 1). TLC run in 1: 1 ethyl acetate: hexane indicate a single spot, Rf 0.10. The desired product was obtained in a yield of 0.29 g (23%). ESI/MS calculated for $C_{34}H_{57}N_4O_7B_1$ - H: 643.2. Found: 643.4.

Example 28

H-Val-Val-Pro-boroAlg-pinanediol ester•HCl

Boc-Val-Val-Pro-boroAlg-$C_{10}H_{16}$, Example 27 (0.23 g, 0.36 mmol) was dissolved in 5 mL 4N HCl in dioxane and stirred at room temperature for 3 h. Ether was added to yield a white precipitate that was isolated by filtration. After drying over P_2O_5 *in vacuo* the desired product was obtained as a white solid in a yield of 86 mg, 44%). ESI/MS calculated for $C_{29}H_{49}N_4O_5B_1$ + H: 544.4. Found: 545.4.

Example 29

Ac-Val-Val-Pro-boroAlg-pinanediol

H-Val-Val-Pro-boroAlg-$C_{10}H_{16}$•HCl (Example 28, 76 mg, 0.13 mmol) was dissolved in 5 mL methylene chloride. Diisopropylethylamine (46 µL, 0.26 mmol) and acetic anhydride (14 µL, 0.15 mmol) were added and the reaction mixture stirred overnight at room temperature. The mixture was washed with 0.20 N HCl, 5% $NaHCO_3$, and saturated aqueous NaCl. The organic phase was dried over sodium sulfate, filtered and concentrated to yield a yellow oil (41 mg, 54%). ESI/MS calculated for $C_{31}H_{51}N_4O_6B_1$ + H: 587.4. Found: 587.4.

Example 30

Glut-Val-Val-Pro-boroAlg-pinanediol

H-Val-Val-Pro-boroAlg-$C_{10}H_{16}$•HCl (Example 28, 100 mg, 0.18 mmol) was dissolved in methylene chloride (10 mL). Glutaric anhydride (19 mg, 0.17 mmol) and diisopropylethylamine (63 µL, 0.36 mmol) were added. The reaction mixture stirred at room temperature overnight. The reaction mixture was washed with 0.20 N HCl and the organic phase was dried over Na_2SO_4, filtered, and concentrated in vacuo to yield a oil. The oil was triturated from hexane to yield a white solid which was further purified by HPLC using C18 Rainin, 4 x 30 cm, column. A gradient from 55% acetonitrile in water to100% acetonitrile was ran to yield 16 mg of the desired product. ESI/MS calculated for $C_{34}H_{55}N_4O_8B_1$+H: 659.4. Found: 659.4.

Example 31

Boc-Asp(O^tBu)-D-Glu(O^tBu)-Val-Val-Pro-boroAlg-pinanediol

This Example was prepared was prepared according to the procedure described for Example 9 except Z-D-Glu(O^tBu)-OH was used in place of the Z-Glu(O^tBu)-OH. ESI/MS calculated for $C_{51}H_{86}N_6O_{13}B_1$ +H: 1001.6. Found: 1001.8.

Example 32

Asp-D-Glu-Val-Val-Pro-boroAlg-pinanediol

Boc-Asp(O^tBu)-D-Glu(O^tBu)-Val-Val-Pro-boroAlg-$C_{10}H_{16}$ (49.0 mg, 0.049 mmol) was dissolved in 2 mL of 4 N HCl in dioxane and stirred at room temperature for 2 h. The reaction mixture was concentrated in vacuo to yield an oil which was then purified by HPLC using a 250 x 21.2 mm, Phenomenex,10 µ, C-8 column. Fractions containing the desired product were pooled to yield 12.0 mg (31%). ESI/MS calculated for $C_{38}H_{60}N_6O_{11}B_1$+H: 788.4. Found: 789.5.

Example 33

Ac-Glu(O^tBu)-Val-Val-Pro-boroAlg-pinandiol

The preparation of H-Glu(O^tBu)-Val-Val-Pro-OH is described in the procedure for the preparation of Example 9. H-Glu(O^tBu)-Val-Val-Pro-OH (1.1 g, 2.0 mmol) in 60 mL of 1:1 water: dioxane containing triethylamine (0.55 mL, 3.9 mmol). Acetic anhydride (0.28 mL, 3.0 mmol) was added and the reaction mixture was allowed to stirred overnight at room temperature. The reaction mixture was concentrated approximately 50% by evaporation and then adjusted to pH 1 with HCl. The product was extracted into ethyl acetate and was washed with saturated aqueous NaCl to give Ac-Glu(O^tBu)-Val-Val-Pro-OH as a white solid (1.1 g, 2.0 mmol, 100%). ESI/MS calculated for $C_{26}H_{44}N_4O_8$ + Na: 563.3. Found: 563.3.

Using the procedure described in the preparation of Example 6, the mixed anhydride of Ac-Glu(O^tBu)-Val-Val-Pro-OH (1.0 g, 1.9 mmol) was prepared in 20 mL DMF and coupled to H-boroAlg-$C_{10}H_{16}$ (Example 1) dissolved in 10 mL of THF. The product was purified by silica gel chromatography. The column was eluted using a stepwise gradient of hexane and ethyl acetate. The product was eluted with 9:1ethyl acetate: methanol. Fractions containing the desired product were concentrated *in vacuo* and lyophilized to yield a white solid (380 mg, 0.5mmol, 26%). ESI/MS calculated for $C_{40}H_{66}N_5O_9B_1$ + Na: 794.5. Found: 794.5.

Example 34

Ac-Glu-Val-Val-Pro-boroAlg-pinandiol

Ac-Glu(O^tBu)-Val-Val-Pro-boroAlg-$C_{10}H_{16}$ (80 mg, 0.10 mmol) was treated with 1 mL of 4 N HCl in dioxane for 3 h. Solvent was evaporated and the residue was dissolved in acetonitrile: water and lyophilized to give a white solid

(78 mg, 100%) ESI/MS calculated for $C_{36}H_{58}N_5O_9B_1$ + Na: 738.4. Found: 738.3.

Example 35

Boc-Val-Val-Pro-boroCpg-pinacol

The preparation of Boc-Val-Val-Pro-OH is described in the synthesis of Example 27. The mixed anhydride of Boc-Val-Val-Pro-OH (1.8 g, 4.3 mmol) was prepared in 10 mL THF by the procedure described for the preparation of Example 6. It was coupled to H-boroCpg-pinacol•HCl dissolved in 10 mL of DMF. The product was purified by silica gel chromatography. The column was eluted with a stepwise gradient of ethyl acetate: hexane and final elution was achieved with 9:1 ethyl acetate: methanol. The pooled fractions were concentrated *in vacuo* and lyophilized to yield a white solid 0.64 g (25%). ESI/MS calculated for $C_{30}H_{53}N_4O_7B_1$ + H: 593.4. Found: 593.5.

Example 36

H-Val-Val-Pro-boroCpg pinacol•HCl

Boc-Val-Val-Pro-boroCpg-pinacol (Example 35, 0.36 g, 0.61 mmol) was dissolved in 8 mL of 4 N HCl in dioxane. After stirred at room temperature for 4 h, solvent was evaporated and the residue was triturated with hexane to give a white solid (0.28 g, 0.57 mmol, 93%). ESI/MS calculated for $C_{25}H_{45}N_4O_5B_1$+H: 493.4. Found: 493.5.

Example 37

Glut -Val-Val-Pro-boroCpg-pinanediol

H-Val-Val-Pro-boroCpg pinacol ester (Example 36, 78 mg, 0.15 mmol) was dissolved in water (10 mL) and glutaric anhydride (17.5 mg, 0.15 mmol) was dissolved in dioxane (10 mL) and was added. Sodium bicarbonate (38 mg, 0.45 mmol) was added and the reaction mixture was allowed to stir

until the amine could not be detected by TLC. Pinanediol (51 mg, 0.30 mmol) and the reaction mixture was stirred for 1 h. It was acidified with 1 M HCl prepared in saturated aqueous NaCl. The product was extracted into ethyl acetate, dried over $MgSO_4$, filtered and concentrated in vacuo to yield a clear oil. It was purified by HPLC using C-18 Rainin reverse phase (4 x 30 cm) column with a gradient from 95:5 water/acetonitrile to 5:95 water acetonitrile over 31 minutes (All solvents contained 0.10% TFA). The isolated product was lyophilized from acetonitrile/water to yield a white solid (25.1 mg, 0.04 mmol, 25%) ESI/MS calculated for $C_{34}H_{55}N_4O_8B_1$+H: 659.4. Found: 659.5.

Example 38

Ac-Val-Val-Pro-boroCpg-pinacol

H-Val-Val-Pro-boroCpg-C_6H_{12}•HCl (100 mg, 0.19 mmol) was dissolved in methylene chloride (10 mL) and acetic anhydride (16.1 µL, 0.17 mmol) and diisopropylethylamine (65.8 µL, 0.38 mmol) were added. The reaction mixture was stirred overnight at room temperature and was then concentrated to an oil in vacuo. The oil was purified by HPLC using C-18 Rainin reverse phase (4 x 30 cm) column with a gradient from 95:5 water/acetonitrile to 5:95 water/acetonitrile over 31 minutes (All solvents contained 0.10% TFA). The isolated product was lyophilized from acetonitrile/water to yield a white solid (10.4 mg). ESI/MS calculated for $C_{27}H_{47}N_4O_6B_1$+H: 534.4. Found: 534.4.

Example 39

Boc-Asp(O^tBu)-Glu(O^tBu)-Val-Val-Pro-boroDfb-pinanediol

The mixed anhydride of Boc-Asp(O^tBu)-Glu(O^tBu)-Val-Val-Pro-OH (1.24 g, 1.61 mmol) was prepared in 10 mL of THF by the procedure described for Example 6 and was coupled to

boroDfb-pinanediol (Example 4) dissolved in 5 mL of THF. Following purified on a 5 x 90 cm column of Sephadex™ LH-20 column using as a solvent methanol, the desired product as an amorphous solid (0.51 g, 30.9%) was obtained. TLC in 100 % ethyl acetate indicated the product as a single spot with R_F of 0.45. ^{1}H-NMR ($CDCl_3$) δ 7.02 (m, 2H), 6.21-5.82 (m, 1H), 5.63 (m, 2H), 4.73-4.10 (m, 7H), 3.81 0 3.60 (m, 3H), 2.95 (m, 1H), 2.82-1.61 (m, 20H), 1.46-1.40 (3s, 27H), 1.23 (s, 3H), 1.30 (s, 3H), 0.95 (m, 15H). ESI/MS calculated for $C_{50}H_{82}N_6O_{13}F_2B_1$ +H: 1025.6. Found 1025.6.

Example 40

H-Asp-Glu-Val-Val-Pro-boroDfb pinanediol ester• hydrochloride

The hexapeptide analog, Example 39, (0.26 g, 0.25 mmol) was treated with 4 N HCl in dioxane (5 mL) for 3 h. The material was concentrated *in vacuo* and a sample (40 mg) was purified by HPLC using C-8 Phenomenex reverse phase (2.1 x 25 cm) column using a water: acetonitrile gradient (All solvents were adjusted to 0.1% TFA.). The product eluted at 80% acetonitrile. The fractions were evaporated and dried under high vacuum to obtain 10.1 mg (25.3 %) of the desired product as a white amorphous solid. ^{1}H-NMR (CD_3OD) δ 6.21-5.80 (m, 1H), 4.62-4.05 (m, 7H), 3.98 (m, 1H), 3.65 (m, 1H), 3.02 (dd, 1H), 2.82 (m 2H), 2.61-1.78 (m, 20H), 1.42 (m, 2H), 1.31 (s, 3H), 1.28 (s, 3H), 0.98 (m, 15H). ESI/MS calculated for $C_{37}H_{59}N_6O_{11}F_2B$ +H: 813.5. Found 813.5.

Example 41

Boc-Val-Val-Pro-boroDfb pinanediol ester.

The mixed anhydride of Boc-Val-Val-Pro-OH (0.16 g, 0.39 mmol) was prepared in THF (5 mL) and was coupled to H-boroDfb-pinanediol•HCl (Example 4, 0.12 g, 0.39 mmol) dissolved in $CHCl_3$ (10 mL) using the procedure in Example

6. After purification by silica gel chromatography using ethyl acetate as a solvent, the desired product was obtained as an amorphous solid (44 mg). ^{1}H-NMR ($CDCl_3$) δ 7.08 (d, 1H), 6.75 (d, 1H), 5.05 (d, 1H), 4.63-4.21 (m, 5H), 3.81-3.58 (m, 2H), 3.0 (m, 1H), 2.56-1.62 (m, 12H), 1.44 (s, 9H), 1.32 (s, 3H), 1.24 (s, 3H), 0.95 (m, 15H). ESI/MS calculated for $C_{33}H_{55}F_2N_4O_7B_1$ + H: 669.6. Found: 669.6.

Example 42

Boc-Hyp(Bzl)-boroDfb-pinanediol.

The mixed anhydride of Boc-Hyp(OBzl)-OH (0.66 g, 2.06 mmol) in 5 mL THF using the procedure described in Example 6. After 5 minutes, 1-amino-3,3-difluoropropane-1-boronate pinanediol ester (0.64 g, 2.06 mmol) dissolved in THF (5 mL) was added to this mixture at -20 ^{0}C. Cold THF was used to aid in the transfer. Triethylamine (0.29 mL), 2.06 mmol) was added and the reaction mixture was allowed to come to room temperature and to stir overnight. The mixture was filtered and the solvent was removed by evaporation. The residue was dissolved in ethyl acetate, washed with 0.2 N HCl, 5% $NaHCO_3$ and saturated NaCl. The organic phase was dried with Na_2SO_4, filtered and evaporated to yield a dark brown oil. The crude product was purified on silica gel. The column was eluted using a stepwise gradient of ethyl acetate: hexane from a ratio of 10: 90 to a ratio of 1: 1. TLC in ethyl acetate: hexane 1: 1 indicated the product at R_F of 0.34. Fractions containing the product were concentrated *in vacuo* to give 82.2 mg (7.0 %) of 1. ^{1}H NMR ($CDCl_3$) δ 7.26 (m, 5H), 6.18 - 5.62 (m, 1H), 4.41 (s, 2H), 4.4.25 (m, 1H)m 4.19 (d, 1H), 3.38 (m, 2H), 3.0 (m, 1H), 2.41 m- 1.72 (m, 10H), 1.41 (s, 9H), 1.32 (s, 3H), 1.21 (s, 3H), 0.81 (s, 3H). (ESI/MS) calculated for $C_{30}H_{43}N_2O_6F_2B_1$ +H: 577.3. Found 577.3.

Example 43

Pz-CO-Val-Val-Hyp(Bzl)-boroDfb-pinanediol.

H-Hyp(OBzl)-boroDfb-pinanediol•HCl. Boc-Hyp(OBzl)-boroDfb-pinanediol (Example 42, 52.2 mg, 0.090 mmol) was dissolved in 5 mL of 4M HCl in dioxane and stirred under nitrogen for two hours. The reaction mixture was concentrated *in vacuo* and dried under vacuum to give 48.8 mg (73.3 %) of the desired product. ESI/MS) calculated for $C_{25}H_{34}N_2O_4F_2B_1$ +H: 477.3. Found: 477.3.

H-Hyp(OBzl)-boroDfb-pinanediol•HCl (0.049 g. 0.095 mmol), Pz-CO-Val-Val-OH, from Example 18, (0.034 g, 0.095 mmol), HOBT (0.026 g, 0.19 mmol), and NMM (0.010 mL, 0.095 mmol) were dissolved in 5 mL of chloroform and DCC (0.019 g, 0.095 mmol)was added. The reaction mixture was stirred overnight at room temperature. The mixture was filtered and solvent was evaporated. Ethyl acetate was added and insoluble material was removed by filtration. The filtrate was washed with 0.2N HCl, 5% $NaHCO_3$ and saturated aqueous NaCl. It was dried over Na_2SO_4, filtered and evaporated to give a brown oil. The crude product was purified on silica gel. The column was eluted using a stepwise gradient of ethyl acetate: hexane from a ratio of 20: 80 to a ratio of 80: 20. TLC in ethyl acetate: hexane 1: 1 indicated the product at R_F of 0.31. Fractions containing the product were concentrated *in vacuo* to give 7.1 mg (10.0 %) of the desired tetrapeptide analog. ^1H NMR ($CDCl_3$) δ 9.38 (d, 1H), 8.78 (d, 1H), 8.56 (m, 1H), 8.41 (d, 1H), 8.00 (m, 1H), 7.78 (m, 1H), 7.25 (m, 5H), 6.10 - 5.75 (m, 1H), 4.78 (m, 2H), 4.61 (t, 1H), 4.42 (q, 2H), 4.22 (m, 1H), 4.18 (d, 1H), 3.62 (dd, 1H), 3.18 (m, 2H), 2.99 (m, 1H), 2.31 - 1.35 (m, 10H), 1.23 (s, 3H), 1.9 (s, 3H), 0.98 - 0.81 (m, 15H). (ESI/MS) calculated for $C_{40}H_{55}N_6O_7F_2B_1$ +Na: 803.4. Found 803.4.

Example 44

Preparation of Ac-Asp(OBzl)-Leu-Glu(OBzl)-Val-Val-boroThr(OBzl)Pinanediol

Ac-Asp(OBzl)-Leu-Glu(OBzl)-Val-Va-OH. Z-Val-Val-OtBu was prepared by coupling Z-Val-OH and H-Val-O^{t}Bu. Z-Val-OH (11.9 g, 47.7 mmol), H-Val-O^{t}Bu·HCl (10.0 g, 47.7 mmol) and 1-hydroxybenzotriazole (12.8 g, 95.4 mmol) were dissolved in chloroform (300 mL). N-Methylmorpholine (NMM, 5.24 mL, 47.7 mmol) and N,N'-dicyclohexylcarbodiimide (DCC, 9.83 g, 47.7 mmol) were added and the reaction mixture was allowed to stir overnight at room temperature. The reaction mixture was filtered and the solvent was evaporated. The residue was dissolved in ethyl acetate (200 mL) and refiltered. The filtrate was washed with 0.20 N HCl, 5% $NaHCO_3$, and saturated aqueous NaCl. The resulting solution was dried over Na_2SO_4, filtered, and concentrated in vacuo to give 18.2 g (94 %) of the desired product as a viscous oil. ^{1}H-NMR ($CDCl_3$) 7.33 (m, 5H), 6.47 (d, 1H), 5.55 (d, 2H), 5.10 (s, 2H), 4.41 (dd, 1H), 4.07 (t, 1H), 2.12 (m, 2H), 1.45 (s, 9H), 0.97-0.84, (m, 12H). ESI/MS calculated for $C_{22}H_{34}N_2O_5$ + Na: 429.2. Found: 429.3.

H-Val-Val-O^{t}Bu was prepared by dissolving Z-Val-Val-O^{t}Bu (18.2 g, 44.8 mmol) in methanol (300 mL) containing 1% acetic acid. Palladium on carbon (300 mg) was added and the flask was placed on the Parr hydrogenation apparatus under an initial H_2 pressure of 50 psi and the mixture was hydrogenated for a total of 36 h while refilling the Parr bottle as needed. The catalyst was removed by filtration through a celite bed. The filtrate was concentrated in vacuo to give H-Val-Val-O^{t}Bu (12.3 g , 45.2 mmol) ^{1}H-NMR 4.20 (d, 1H), 3.60 (d, 1H), 2.13 (m, 2H), 1.47 (s, 9H), 1.06-0.97 (m, 12H). MS/ESI calculated for $C_{14}H_{29}N_2O_3$: 273.2. Found 273.3

Boc-Glu(OBzl)-Val-Val-O-^{t}Bu was prepared by coupling H-Val-Val-O-^{t}Bu and Boc-Glu-(OBzl)-OH. H-Val-Val-O-^{t}Bu·AcOH (12.4

g, 37.3 mmol), Boc-Glu(OBzl)-OH (12.5 g, 37.3 mmol) and 1-hydroxybenzotriazole (10.1 g, 74.6 mmol) were dissolved in chloroform (500 mL). NMM (4.10 ml, 37.3 mmol) and N,N'-dicyclohexylcarbodiimide (DCC, 7.69 g, 37.3 mmol) were added and the reaction mixture was allowed to stir overnight at room temperature. The reaction mixture was filtered and the solvent was concentrated. The residue was dissolved in ethyl acetate (200 mL) and refiltered. The filtrate was washed with 0.20 N HCl, 5% $NaHCO_3$, and saturated aqueous NaCl. The resulting solution was dried over anhydrous Na_2SO_4, filtered, and concentrated in vacuo to give 15.4 g (69 %) of the desired product as an opaque glass. 1H-NMR ($CDCl_3$) 7.35 (m, 5H), 6.84 (d, 1H) 6.48 (d, 1H), 5.37 (d, 1H), 5.12 (s, 2H), 4.40 (dd, 1H), 4.29 (t, 1H), 4.20 (m, 1H), 2.51 (m, 2H), 2.16-1.91 (m, 4H), 1.45 (s, 9H), 1.43 (s, 9H), 0.96-0.87 M, 12H). MS/ESI calculated for $C_{31}H_{49}N_3O_8$: 592.3. Found: 592.2.

H-Glu(OBzl)-Val-Val-O-tBu•HCl was prepared by adding Benzenesulfonic acid (1.95 g, 12.3 mmol) to a solution of Boc-Glu(OBzl)-Val-Val-O^{t}Bu (6.10 g, 10.3 mmol) in 1,4-dioxane (300 mL) and the resulting solution was heated at 60°C for 8 h. The solution was evaporated, redissolved in CH_2Cl_2 (300 mL), washed with 5% aqueous $NaHCO_3$, and to the resulting solution was added an ethereal solution of HCl (1N, 8 mL). This solution was dried over Na_2SO_4 and concentrated to yield 2.38 g of a white foam (47%). ^{1}H-NMR (CD_3OD) 7.31 (m, 5H), 5.11 (s, 2H), 4.25 (d, 1H), 4.15 (d, 1H), 4.02 (t, 1H), 2.52 (t, 2H), 1.44 (s, 9H), 2.17-2.02 (m, 4H), 0.99-0.85 (m, 12H). MS/APCI calculated for $C_{26}H_{43}N_3O_6$ + H^+: 493.3. Found: 493.5.

Ac-Asp(OBzl)-OH was prepared by adding triethylamine (6.86 mL, 49.3 mmol) to a suspension of H-Asp(OBzl)-OH (5.00 g, 22.4 mmol) in a 1:1 water: dioxane (200 mL). Acetic anhydride was added to this solution and the resulting mixture was allowed to stir for 18 h. The dioxane was

removed via rotary evaporation and the pH was lowered to 1 with 1.0 N HCl. The heterogeneous solution was extracted with ethyl acetate (3 x 100 mL). The combined organic extracts were washed with brine, dried over Na_2SO_4, and concentrated to yield 5 g (84%) of a white semi-solid. ^{1}H-NMR ($CDCl_3$) 7.33 (m, 5H), 6.77 (br s, 1H), 5.12 (s, 2H), 4.87 (m, 1H), 3.10 (qd, 2H), 2.01 (s, 3H). MS/ESI calculated for $C_{13}H_{15}NO_5$ -H: 264.1. Found: 264.1.

Ac-Asp(OBzl)-Leu-O^{t}Bu was prepared by coupling Ac-Asp-(OBzl)-OH and H-Leu-OtBu. Ac-Asp-(OBzl)-OH (5.1 g, 19.2 mmol), H-Leu-O^{t}Bu·HCl (4.31 g, 19.2 mmol) and 1-hydroxybenzotriazole (5.22 g, 38.5 mmol) were dissolved in chloroform (300 mL). N-Methylmorpholine (NMM, 2.12 mL, 19.2 mmol) and N,N'-dicyclohexylcarbodiimide (DCC, 3.97 g, 19.2 mmol) were added and the reaction mixture was allowed to stir overnight at room temperature. The reaction mixture was filtered and the solvent was concentrated. The residue was dissolved in ethyl acetate (200 mL)1 and refiltered. The filtrate was washed with 0.20 N HCl, 5% NaHCO3, and saturated aqueous NaCl. The resulting solution was dried over Na_2SO_4, filtered, and concentrated in vacuo to give 7.31 g (94 %) of the desired product as a viscous oil. ^{1}H-NMR ($CDCl_3$) 7.34 (m, 5H), 5.12 (m, 2H), 4.85 (m, 1H), 4.40 (m, 1H), 2.83 (dd, 2H), 1.99 (s, 3H), 160-1.45 (m, 3H) 1.44 (s, 18H), 0.94 - 0.88 (m, 12H). MS/ESI calculated for $C_{23}H_{34}N_2O_6$ + H: 435.2. Found: 435.3.

Ac-Asp(OBzl)-Leu-OH was prepared by dissolving Ac-Asp(OBzl)-Leu-O^{t}Bu (13.5 g, 31.0 mmol) in 4 N HCl (50 mL) in 1,4-dioxane and the solution was allowed to stir at room temperature for 16 h. The solution was concentrated under reduced pressure yielding 9.9 g (84%) of a yellow foam ^{1}H-NMR ($CDCl_3$) 7.27 (m, 5H), 5.05 (m, 2H), 4.92 (m, 1H), 4.42 (m, 1H), 2.77 (m, 2H), 1.91 (s, 3H), 1.57 (m, 3H), 0.88 (m, 12H). MS/ESI calculated for $C_{19}H_{26}N_2O_6$ - H: 377.4. Found: 377.2.

Ac-Asp(OBzl)-Leu-Glu(OBzl)-Val-Val-O^{t}Bu was prepared by coupling Ac-Asp(OBzl)-Leu-OH and H-Glu-(OBzl)-Val-Val-OH. Ac-Asp(OBzl)-Leu-OH (2.38 g, 4.5 mmol), H-Glu(OBzl)-Val-Val-O^{t}Bu•HCl (1.70 g, 4.5 mmol) and 1-hydroxybenzotriazole (1.22 g, 9.0 mmol) were dissolved in chloroform (300 mL). N-Methylmorpholine (NMM, 0.81 mL, 4.5 mmol) and N,N'-dicyclohexylcarbodiimide (DCC, 0.93 g, 4.5 mmol) were added and the reaction mixture was allowed to stir overnight at room temperature. The reaction mixture was filtered and the solvent was concentrated. The residue was dissolved in ethyl acetate (200 mL)1 and refiltered. The filtrate was washed with 0.20 N HCl, 5% $NaHCO_3$, and saturated aqueous NaCl. The resulting solution was dried over Na_2SO_4, filtered and concentrated in vacuo to give 2.6 g (68 %) of the desired product as a pale yellow powder. ^{1}H-NMR ($CDCl_3$) (7.31 (m, 10H), 5.04 (m, 4H), 4.90 (m, 1H) 4.36-4.01 (m, 4H), 4.40 (m, 1H) 2.82 (m, 2H), 2.38 (m, 2H),), 2.06-0.99 (m , 15H), 1.37 (s, 9H), 0.85-0.76 (m, 12H). MS/ESI calculated for $C_{45}H_{65}N_5O_{11}$ + Na: 874.5. Found: 874.5.

Ac-Asp(OBzl)-Leu-Glu(OBzl)-Val-Val-OH was prepared by dissolving Ac-Asp(OBzl)-Leu-Glu(OBzl)-Val-Val-O^{t}Bu (3.1 g, 3.6 mmol) in 4 N HCl (20 mL) in 1,4-dioxane and the solution was allowed to stir at room temperature for 20 h. The solvent was concentrated *in vacuo* to yield 1.2 g of a yellow oil. This material, in 200 mg portions, was further purified by preparative HPLC using a 4 x 30 cm Rainin C-18 reverse phase column. A gradient from 60:40 acetonitrile: water to 100% acetonitrile was run over a period of 45 min at a flow rate of 40 mL/min. The fractions eluting at 8.7 min were combined to yield a 0.44 g (15%) of a white amorphous solid. ^{1}H-NMR ($CDCl_3$) 7.25 (m, 10H), 5.02 (m, 4H), 4.74 (t, 1H), 4.36-4.26 (m, 4H), 4.13 (t, 1H), 3.37 (m, 1H), 2.79 (d, 2H), 2.36 (t, 2H), 2.14-0.99 (m, 14H),

0.86-0.78 (m, 12H). MS/ESI calculated for $C_{41}H_{57}N_5O_{11}$ - H: 794.4. Found: 794.3.

Ac-Asp(OBzl)-Leu-Glu(OBzl)-Val-Val-boroThr(OBzl)-$C_{10}H_{16}$ was prepared by coupling the protected pentapeptide to H-boroThr(OBzl)-pinanediol (Example 5b). Ac-Asp(OBzl)-Leu-Glu(OBzl)-Val-Val-OH (0.31 g, 0.39 mmol) was dissolved in THF (20 mL) and cooled to -20°C. NMM (44 •L, 0.39 mmol) and isobutylchloroformate (56 •L, 0.39 mmol) were added. After 5 min, a solution of H-boroThr(OBzl)-pinanediol•HCl(0.22 g, 0.59 mmol) in THF (10 mL) at -20°C was added. Cold THF (5 mL) was used to aid in the transfer. Triethylamine (57 •L, 0.39 mmol) was added and the reaction was allowed to warm to room temperature while stirring overnight. The solvent was removed by evaporation, redissolved in ethyl acetate (100 mL), washed with 0.2 HCl, 5% $NaHCO_3$, and saturated NaCl. The organic phase was dried with Na_2SO_4, filtered, and evaporated to yield a brown oil. This material was further purified by chromatography on a 2.5 x 90 cm column of Sephadex™ LH-20 in methanol. Fractions 20-30 were collected (10mL/fraction, 3 mL/min) to yield 127 mg of a white solid. This solid was finally purified by preparative HPLC using a 4 x 30 cm Rainin C-18 reverse phase column. A gradient of 0% acetonitrile to 100 % acetonitrile was run over a period of 45 min. The product eluted at 28.9 min. The fractions were evaporated to yield 80 mg (18%) of a white amorphous solid. ^{1}H-NMR (CD_3OD) d 7.25 (m, 15H), 5.04 (m, 5H), 4.59-4.34 (m, 8H) 4.07 (m, 2H), 3.9 (d,1H), 2.34-2.00 (m, 7H), 1.87 (s, 3H), 1.25-1.19 (m, 14 H), 1.11 (d, 3H) 0.91-0.78 (m, 21H). MS/ESI calculated for $C_{61}H_{85}BN_6O_{13}$ + H: 1121.6. Found: 1121.6

Example 45

Preparation of Ac-Asp-Leu-Glu-Val-Val-boroThr-$C_{10}H_{16}$

Ac-Asp-Leu-Glu-Val-Val-boroThr-$C_{10}H_{16}$ was prepared by hydrogenation of Ac-Asp(OBzl)-Leu-Glu(OBzl)-Val-Val-boroThr(OBzl)-$C_{10}H_{16}$ in MeOH (20 mL). Pearlman's catalyst $Pd(OH)_2$ (10 mg) was added and the flask was placed on the Parr hydrogenation apparatus under an initial H_2 pressure of 35 psi. The solution was hydrogenated for 3 h. The catalyst was removed by filtration through a celite pad. The filtrate was evaporated in vacuo to give a white solid. The compound was purified by HPLC using a C-18 reverse phase (2.5 x 25 cm) column with a gradient starting at 0% acetonitrile and going to 100% acetonitrile over a period of 25 min. The product eluted at 20.1 min. The solvent was evaporated to yield a residue that was lyophilized to yield 20 mg (55%) of a white amorphous solid. ^{1}H-NMR (CD_3OD) d 4.06 (t, 1H), 4.38 (m, 3H), 3.88 (m, 2H), 2.73 (dd, 2H), 2.34 (m, 2H), 2.09 (m, 2H), 1.98 (s, 3H), 1.96-1.39 (m, 8H), 1.38 (d, 3H), 1.29 (d, 3H), 1.23 (d, 3H), 0.99-0.88 (m , 21H). MS/ESI calculated for $C_{40}H_{67}BN_6O_{13}$ -H: 849.5. Found: 849.5.

Example 46

Preparation of Boc-Asp(OtBu)-Glu(OtBu)-Val-Val-Pro-boroSer(OBzl)-Pinanediol

Boc-Asp(O^tBu)-Glu(O^tBu)-Val-Val-Pro-boroSer(OBzl)-$C_{10}H_{16}$ was prepared by coupling the protected pentapeptide to H-boroSer(OBzl)-$C_{10}H_{16}$ (Example 5c). Boc-Asp(O^tBu)-Glu(O^tBu)-Val-Val-Pro-OH (1.0 g, 1.3 mmol) was dissolved in DMF (5 mL) and cooled to -20°C. NMM (154 •L, 0.39 mmol) and isobutylchloroformate (182 •L, 1.3 mmol) were added. After 5 min, a solution of H-boroSer(OBzl)-$C_{10}H_{16}$•HCl (0.48 g, 1.30 mmol) in THF (10 mL) at -20°C was added. Cold THF (5 mL) was used to aid in the transfer. Triethylamine (192 •L, 1.30 mmol) was added and the reaction was allowed to warm to room temperature while stirring overnight. The solvent was removed by evaporation, redissolved in ethyl acetate (100 mL), washed with 0.2 N HCl, 5% $NaHCO_3$, and

saturated NaCl. The organic phase was dried with Na_2SO_4, filtered, and evaporated to yield a clear glass. This was further purified by silica gel column chromatography (ethyl acetate eluant). This solid was finally purified by preparative HPLC using a 4 x 30 cm Rainin C-18 reverse phase column, 210 nm detection, 40 mL/min. A gradient of 75% acetonitrile to 100 % acetonitrile was run over a period of 45 min. The product eluted at 23.7 min. The fractions were evaporated to yield 400 mg (28.5 %) of a white amorphous solid. ^{1}H-NMR ($CDCl_3$) δ 7.30 (m, 5H), 4.45 (d, 1H), 3.78 (s, 1H) 3.58 (s, 2H), 2.67 (m, 3H), 2.34-2.00 (m, 7H), 2.40-1.68 (m, 16H), 1.45 (s, 9H) 1.43 (s, 9H),1.41 (m, 9H),1.29 (s, 3H), 1.25 (s, 3H) 0.91-0.83 (m, 15H). MS/ESI calculated for $C_{56}H_{89}N_6BO_{14}$+ H^+: 1081.7. Found: 1081.7.

Example 47

Preparation of Boc-Asp(O^tBu)-Glu(O^tBu)-Val-Val-Pro-boroSer-pinanediol.

Boc-Asp(O^tBu)-Glu(O^tBu)-Val-Val-Pro-boroSer-pinanediol was prepared by catalytic hydrogenation of Boc-Asp(O^tBu)-Glu(O^tBu)-Val-Val-Pro-boroSer(OBzl)-pinanediol. Boc-Asp(O^tBu)-Glu(O^tBu)-Val-Val-Pro-boroSer(OBzl)-pinanediol (112 mg, 0.104 mmol) was dissolved in MeOH (150 mL). Pearlman's catalyst $Pd(OH)_2$ (50 mg) was added and the compound was hydrogenated on a Parr apparatus. After hydrogen consumption was complete, the catalyst was removed by filtration through a celite pad and the filtrate was evaporated to yield a white solid. This solid was further purified by preparative HPLC using a 4 x 30 cm Rainin C-18 reverse phase column, 210 nm detection, and a flow rate of 40 mL/min. A gradient from 0% acetonitrile to 100 % acetonitrile was run over a period of 45 min. The product eluted at 28.4 min to yield 45 mg (44%) of a white solid. ^{1}H-NMR ($CDCl_3$) d 4.56 (m, 3H), 4.05 (d, 1H), 3.82-3.47 (m, 4H), 2.81-1.33 (m, 20H), 1.40 (s, 9H), 1.36 (s, 9H), 1.33

(s, 9H), 1.23 (s, 3H), 1.18 (s, 3H) 0.86-0.76 (m, 15H). MS/ESI calculated for $C_{49}H_{83}N_6BO_{14}$+ Na^+: 1013.6. Found: 1013.6.

Example 48

Preparation of H-Asp-Glu-Val-Val-Pro-boroSer(OBzl)-pinanediol·HCl

This compound was prepared by dissolving Boc-Asp(O^tBu)-Glu(O^tBu)-Val-Val-Pro-boroSer(OBzl)-pinanediol (126 mg, 0.12 mmol) in a solution of HCl in dioxane (4 N, 5 mL). The solution was stirred for 3 h at room temperature under N_2. The solvent was removed by evaporation and the material was purified by preparative HPLC using a 4 x 30 cm Rainin C-18 reverse phase column (210 nm detection, 40 mL/min). A gradient of 0% acetonitrile to 100% acetonitrile (all solvents containd 0.1% TFA) was run over a period of 40 min. The product eluted at 22.3 min to yield 87 mg (83%) of a white solid. ^{1}H-NMR (CD_3OD) δ 7.34 (m, 5H), 4.61 (m, 1H) 4.50 (m, 3H), 4.31 (m, 2H), 4.11 (d, 1H), 3.94 (m, 2H), 3.72 (m, 2H), 3.56 (m, 1H), 3.41 (t, 1H), 3.03-2.77 (m, 3H), 2.40 (t, 2H), 2.33-1.66 (m, 14H), 1.28 (s, 3H), 1.26 (s, 3H), 0.99-0.84 (m, 15H). MS/ESI calculated for $C_{43}H_{65}N_6BO_{12}$+ H^+: 869.5. Found 869.7.

Example 49

Preparation of H-Asp-Glu-Val-Val-Pro-boroSer-pinanediol·HCl

H-Asp-Glu-Val-Val-Pro-boroSer-pinanediol was prepared by catalytic hydrogenation of H-Asp-Glu-Val-Val-Pro-boroSer(OBzl)-pinanediol (Example 48). H-Asp-Glu-Val-Val-Pro-boroSer(OBzl)-pinanediol·HCl (25 mg, 0.028 mmol) was dissolved in MeOH (50 mL). Pearlman's catalyst $Pd(OH)_2$ (5 mg) was added and the compound was hydrogenated on a Parr apparatus. After hydrogen consumption was complete, the catalyst was removed by filtration through a celite pad and the filtrate was evaporated to yield a white solid. This

solid was further purified by preparative HPLC using a 2.2 x 25 cm Vydac C-18 reverse phase column using 210 nm detection and a flow rate of 8 mL/min). A gradient of 0% acetonitrile to 100 % acetonitrile (all solvents contained 0.1% TFA) was run over a period of 45 min. The product eluted at 16.1 min to yield 5 mg (21%) of a white solid. ^{1}H-NMR (CD_3OD) δ 4.93 (m, 1H), 4.78 (m, 1H), 4.60 (m, 1H), 4.40 (m, 3H), 4.16 (m, 3H), 3.68 (m, 2H), 3.48 (m, 1H), 2.93 (m, 1H), 2.76 (m, 2H), 2.33-1.66 (m, 14H), 1.26 (s, 3H), 1.25 (s, 3H), 0.96-0.83 (m, 15H). MS/ESI calculated for $C_{36}H_{59}N_6BO_{12}$+ H^+: 779.4. Found: 779.5.

Example 50

Preparation of Pz-CO-Val-Val-Pro-boroAlg-$C_{10}H_{16}$.

Boc-Pro-boroAlg-C10H16 was prepared by coupling Boc-Pro-OH to H-boroAlg-$C_{10}H_{16}$ using the procedure in Example 18 for the analogous reaction. The desired product was obtained in a yield of 88%. ESI *m/z* calculated for $C_{24}H_{39}N_2BO_5$ + H: 447.4. Found: 4474. Boc-Pro-boroAlg-$C_{10}H_{16}$ was deblocked with anhydrous HCl and coupled to Pz-CO-Val-Val-OH using carbodiimide coupling also following the procedure described for Example 18 to give the desired product. ESI *m/z* calculated for $C_{34}H_{51}BN_6O$: 651.6. Found: 651.6.

Example 51

Preparation of Pz-CO-Val-Val-Hyp(OBzl)-boroAlg-$C_{10}H_{16}$ Using the procedure described for Example 50, Boc-Hyp(OBzl)-boroAlg-$C_{10}H_{16}$ was prepared. ESI *m/z* calculated for $C_{26}H_{37}N_2O_4B$: 453.4. Found: 453.4. Pz-CO-Val-Val-OH was coupled to H-Hyp(OBzl)-boroAlg-$C_{10}H_{16}$ to give the desired product. ESI *m/z* calculated for $C_{41}H_{57}BN_6O_7$: 757.8. Found: 757.6.

Example 52

Preparation of Ac-Val-Val-Hyp(OBzl)-boroAbu-$C_{10}H_{16}$.

Boc-Val-Val-OH was prepared by coupling Boc-Val-OH to H-Val-OBzl using DCC and removing the benzyl ester by catalytic hydrogenation. Boc-Val-Val-OH was coupled to H-Hyp(OBzl)-boroAbu-C10H16 (from Example 18) using DCC coupling. This product was deblocked and treated with acetic anhydride to give the N-acetylated product. ESI m/z calculated for $C_{37}H_{57}BN_4O_7$ + Na: 703.4. Found: 703.4.

Example 53

Preparation of Glut-Val-Val-Hyp(OBzl)-boroAbu-$C_{10}H_{16}$.

H-Val-Val-Hyp(OBzl)-boroAbu-$C_{10}H_{16}$ was treated with glutaric anhydride in dichloromethane in the presence of diisopropylethylamine to give the desired product. ESI *m/z* calculated for $C_{40}H_{61}BN_4O_9$ + Na: 775.6. Found: 775.4.

Example 54

Preparation of Pz-CO-Val-Val-Hyp(OBzl)-boroTpa-$C_{10}H_{16}$.

(boroTpa-$C_{10}H_{16}$ is -NH-CH[CH_2-CH_2-CF_3]-BO_2-$C_{10}H_{16}$)

Pyr-Val-Val-Hyp(OBzl)-OH (0.90 g, 1.73 mmol) was dissolved in THF (5 mL) and N-methylmorpholine (0.190 mL, 1.73 mmol) was added. The solution was cooled to -20°C and isobutyl chloroformate (0.22 mL, 1.73 mmol) was added. After 5 min, a cold (-20°C) solution of H-boroTpa-pinacol•HCl (0.5 g, 1.73 mmol) dissolved in $CHCl_3$ (5 mL) was added followed by the addition of triethylamine (0.24 mL, 1.73 mmol). The reaction was allowed to warm to room temperature and stirred overnight. The mixture was filtered and the filtrate was concentrated *in vacuo*. After dissolving the oily residue in ethyl acetate (30 mL), it was washed with 0.2 N HCl, 5 % $NaHCO_3$ and saturated aqueous NaCl. The organic layer was dried over Na_2SO_4 and concentrated. The crude material was tranesterified with pinanediol (4 equivalents) in methanol for 12 h. The crude pinanediol ester was purified on Sephadex™ LH-20 column

(2.5 x 90 cm). TLC in 100 % ethyl acetate indicated the product at R_t of 0.47. Fractions containing the product were concentrated *in vacuo* to give 0.34 g (24.2 %) of product. ^{1}H-NMR ($CDCl_3$) δ 9.38 (d, 1H), 8.78 (d, 1H), 8.56 (m, 1H), 8.41 (d, 1H), 7.25 (m, 5H), 4.78 (m, 2H), 4.61 (t, 1H), 4.42 (m, 2H), 4.22 (m, 1H), 4.18 (d, 1H), 3.62 (dd, 1H), 3.18 (m, 1H), 2.41 - 1.35 (m, 12H), 1.23 (s, 3H), 1.9 (s, 3H), 0.98 - 0.81 (m, 15). (ESI/MS) calculated for $C_{41}H_{56}N_6O_7F_3B_1$ +H 813.6. Found 813.6.

Example 54a

Preparation of Pz-CO-Val-Val-Hyp(OBzl)-boroAsp(O^tBu)-$C_{10}H_{16}$.

Pz-CO-Val-Val-Hyp(OBzl)-OH (0.11g, 0.23 mmol) was dissolved in 5 ml chloroform and NMM (0.025 ml, 0.23 mmol) was added. The solution was cooled to -20 °C and isobutyl chloroformate (0.030 ml, 023 mmol) was added. After 5 min, H-boroAsp(O^tBu)-$C_{10}H_{16}$•HCl (Example 5g, 0.080 g, 0.23 mmol), dissolved in 5 ml of cold THF, and triethylamine (0.031 ml, 0.23 mmol) were added. The reaction mixture was allowed to come to room temperature and to stir overnight. The reaction mixture was filtered and the filtrate evaporated. The residue was dissolved in ethyl acetate and was washed with 5 % $NaHCO_3$, 0.20 N HCl, and saturated aqueous NaCl. After drying over Na_2SO_4, filtering, and evaporating solvent, the residue was chromatogramed on a silica gel column by eluting with 100% ethyl acetate and gradually increasing the polarity to 2% methanol. TLC (100% ethyl acetate) indicated a single spot R_F 0.46. The desired product was obtained as a white solid (0.017g, 8.7 %). ^{1}H NMR ($CDCl_3$) δ 9.40 (d, 1H), 8.79 (d, 1H), 8.60 (d, 1H), 8.52 (d, 1H), 7.39 (s, 5H), 4.82-4.61 (m, 3H), 4.55 (d, 2H), 4.38 (m, 1H), 4.21 (dd, 1H), 4.00 (d, 1H), 3.71 (m, 1H), 3.03 (m, 1H), 2.51-1.82 (m, 8H), 1.42 (s, 9H), 1.31-1.21 (m, 12H), 1.05-0.81 (m, 9H). Analysis calculated for $C_{44}H_{63}BN_6O_9$ + H: 831.6. Found: 831.6.

Example 54b

Preparation of Pz-CO-Val-Val-Hyp(OBzl)-boroAsp-$C_{10}H_{16}$.

Pz-CO-Val-Val-Hyp(OBzl)-boroAsp(O^tBu)-pinanediol (0.010 g, 0.012 mmol) was dissolved in 1 ml dichloromethane. Trifluoroacetic acid (1 ml) was added and the mixture was stirred for 1 h. Solvent was evaporated and the residue was dissolved in water and lyophilized to yield a white solid (0.0034 g, 0.0043 mmol, 37%). ^1H NMR ($CDCl_3$) δ 9.40 (d, 1H), 8.79 (d, 1H), 8.60 (d, 1H), 8.52 (d, 1H), 7.39 (s, 5H), 4.82-4.61 (m, 3H), 4.55 (d, 2H), 4.38 (m, 1H), 4.21 (dd, 1H), 4.00 (d, 1H), 3.80 (m, 1H), 3.05 (m, 1H), 2.51-1.82 (m, 8H), 1.31-1.21(m, 12H), 1.05-0.81 (m, 9H). Analysis calculated for $C_{40}H_{55}BN_6O_9$ - H: 773.5. Found: 773.5.

Example 54d

Preparation of Pz-CO-Val-Val-Hyp(OBzl)-boroGlu(OMe)-$C_{10}H_{16}$.

Pz-CO-Val-Val-Hyp(OBzl)-OH (0.063 g, 0.12 mmol) was dissolved in 3 ml chloroform and NMM (0.013 ml, 0.12 mmol) was added. The solution was cooled to -20°C and isobutyl chloroformate (0.016 ml, 0.12 mmol) was added. After 5 min, H-boroGlu-$C_{10}H_{16}$•HCl (Example 5h, 0.040 g, 0.12 mmol), dissolved in 3 ml of cold THF, and triethylamine (0.015 ml, 0.12 mmol) were added. The reaction mixture was allowed to come to room temperature and to stir overnight. It was filtered and the filtrate evaporated. The residue was dissolved in ethyl acetate and was washed with 5 % $NaHCO_3$, 0.20 N HCl, and saturated aqueous NaCl. After drying over Na_2SO_4, filtering, and evaporating solvent, the desired product was obtained in a yield of 0.080 g (0.090 mmol, 82%). ^1H NMR ($CDCl_3$) δ 9.40 (d, 1H), 8.79 (d, 1H), 8.60 (d, 1H), 8.52 (d, 1H), 7.39 (s, 5H), 4.82-4.61 (m, 3H), 4.55 (d, 2H), 4.38 (m, 1H), 4.21 (dd, 1H), 4.00 (d, 1H),

3.71 (m, 4H), 3.03 (m, 1H), 2.51-1.82 (m, 10H), 1.51-1.21(m, 12H), 1.05-0.81 (m, 9H). Analysis calculated for $C_{42}H_{59}BN_6O_9$ + H: 803.9. Found: 803.9.

Example 54e

Preparation of Pz-CO-Val-Val-Hyp(OBzl)-boroGlu-$C_{10}H_{16}$.

Pz-CO-Val-Val-Hyp(OBzl)-boroGlu-pinanediol (0.10 g, 0.13 mmol) was dissolved in 1 ml dichloromethane. Potassium trimethylsilanolate (0.083 g, 0.65 mmol) was added. The reaction mixture was stirred for 12 h, concentrated and purified by a Sephadex LH-20 column. The desired fractions were pooled and further purified by HPLC using a C4 Vydac column (2.2 x 25 cm) with a linear gradient from 10% acetonitrile: water to 60% acetonitrile (All solvents_contained 0.1% TFA.) run over a time period of 30 min with a flow rate of 8.0 ml/min. The desired product eluted at 24.5 min. Fractions were pooled and lyophilized to yield a white solid (0.034 g, 0.043 mmol, 33%). ^{1}H NMR ($CDCl_3$) δ 9.40 (d, 1H), 8.79 (d, 1H), 8.60 (d, 1H), 8.52 (d, 1H), 7.39 (s, 5H), 4.82-4.61 (m, 3H), 4.55 (d, 2H), 4.38 (m, 1H), 4.21 (dd, 1H), 4.00 (d, 1H), 3.80 (m, 1H), 3.03 (m, 1H), 2.51-1.82 (m, 10H), 1.51-1.21 (m, 12H), 1.05-0.81 (m, 9H). Analysis calculated for $C_{41}H_{57}BN_6O_9$ +H: 787.6. Found: 787.6.

Example 54f

Preparation of Pz-CO-Val-Val-Hyp(OBzl)-boroCys(S-Phenyl)-$C_{10}H_{16}$.

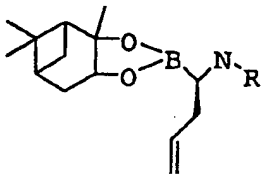
Pz-CO-Val-Val-Hyp(OBzl)-OH (0.21g, 0.41 mmol) was dissolved in 4 ml chloroform and NMM (0.045 ml, 0.41 mmol) was added. The solution was cooled to -20°C and isobutyl chloroformate (0.53 ml, 0.41 mmol) was added. After 5 min, H-boroCys(S-Phenyl)-$C_{10}H_{16}$•HCl (Example 5d, 0.15 g, 0.41 mmol), dissolved in 4 ml of cold THF, and triethylamine (0.055 ml, 0.41 mmol) were added. The reaction mixture was

allowed to come to room temperature and to stir overnight. The reaction mixture was filtered and the filtrate evaporated. The residue was dissolved in ethyl acetate and was washed with 5 % $NaHCO_3$, 0.20 N HCl, and saturated NaCl. After drying over Na_2SO_4, filtering, and evaporating solvent, the residue was chromatogramed on a silica gel column by eluting with 50% ethyl acetate: hexanes and gradually increasing the polarity to 100% ethyl acetate. The desired fractions were pooled and concentrated to give a white solid (0.090 g, 26%). TLC (100 % ethyl acetate) indicated a single spot R_F 0.52. ^1H NMR ($CDCl_3$) δ 9.40 (d, 1H), 8.79 (d, 1H), 8.58 (d, 1H), 8.52 (d, 1H), 7.37 (m, 5H), 4.90 (m, 2H), 4.70 (t, 1H), 4.53 (q, 2H), 4.38-4.04 (m, 3H), 3.71 (m, 1H), 3.38-2.98 (m, 3H), 2.41-1.82 (m, 6H), 1.42 (s, 3H), 1.31 (s, 3H), 0.98-0.81 (m, 15H). Analysis calculated for $C_{45}H_{59}BN_6O_7S$ -H: 837.4. Found: 837.4.

Inhibitor libraries prepared by parallel syntheses are given in the Examples and Tables 2-6 below.

Example 55

Preparation of Ac-boroAlg-$C_{10}H_{16}$ and R-CO-boroAlg-$C_{10}H_{16}$; R-SO_2-boroAlg-$C_{10}H_{16}$ where R is a nonpeptide constituent.

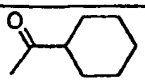
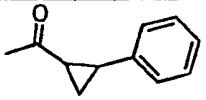


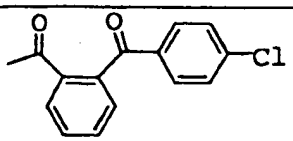
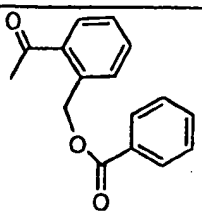
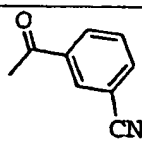
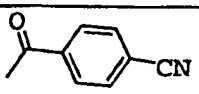
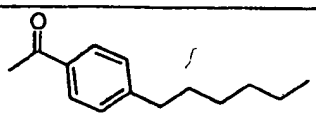
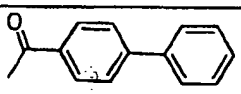
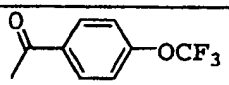
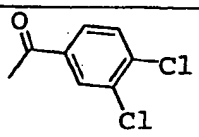
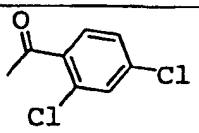
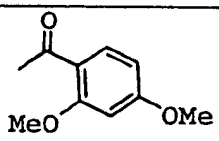
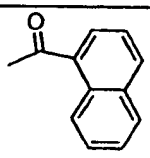
Ac-boroAlg pinanediol ester. H-BoroAlg pinanediol ester, (Example 1, 0.82g, 2.9 mmol) was dissolved in 5 mL of methylene chloride. Acetic anhydride (0.33 mL, 3.4mmol) and diisopropylethylamine (1.0 ml, 5.7 mmol) were added. The reaction mixture stirred overnight at room temperature.

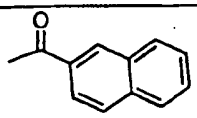
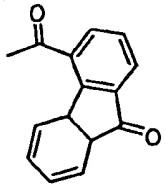
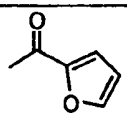
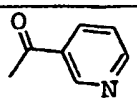
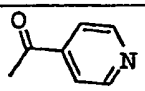
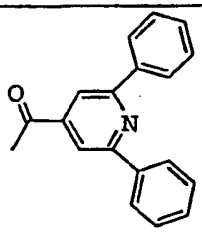
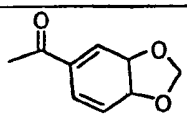
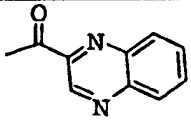
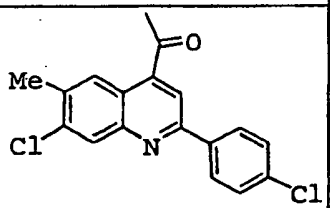
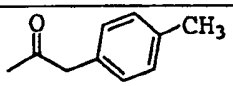
The reaction mixture was washed with 0.2N HCl, 5% $NaHCO_3$, and saturated NaCl solutions. The organic phase was dried over sodium sulfate, filtered and concentrated to yield a yellow oil. This was further purified by silica gel chromatography (hexane/ethyl acetate). The column was equilibrated with 90:10 hexane/ethyl acetate and a gradient was run to 90:10 ethyl acetate/methanol. The pooled fractions were concentrated *in vacuo* to yield an oil which was then lyophilized to yield a white solid (192mg, 0.66mmol, 23%). ESI/MS calculated for $C_{16}H_{26}N_1O_3B_1$: 292.2. Found: 292.3.

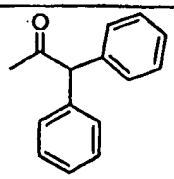
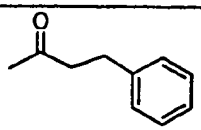
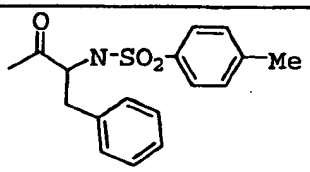
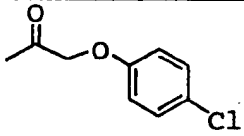
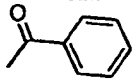
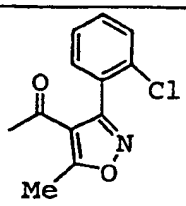
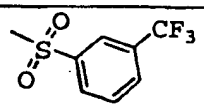
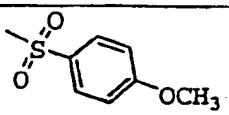
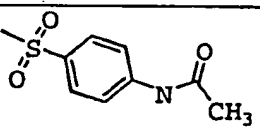
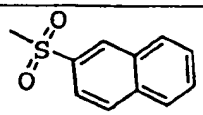
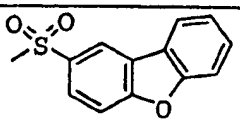
N-Cyclohexanoyl-boroAlg-pinanediol ester. To a glass test tube with screw cap, cyclohexanoyl chloride (3.7 mg, 25 μmol) and ethyl acetate (200 μL) were added. H-boroAlg-$C_{10}H_{16}$•HCl (3.6 mg, 12.5 μmol) in trifluorotoluene (20 μL) was added followed by Amberlite IRA-068 ion exchange resin (~100mg). The resin had been previously washed with methanol and dried over P_2O_5. An additional 200 μL of ethyl acetate was added to the tube. The test tube was capped and placed in a block heater at 55°C on an orbital shaker overnight. Water (100 μL) was added and the tube was returned to the shaken overnight at room temperature. The resin was isolated by filtration and was washed with ethyl acetate. The combined filtrates was evaporated to yield a yellow oil. ESI/MS calculated for $C_{21}H_{34}NO_3B$ +H: 360.3. Found: 360. Compounds in Table 2 were prepared using this procedure.

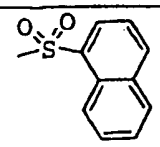
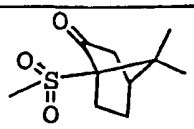
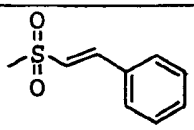
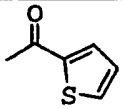
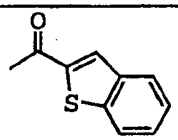
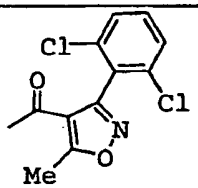
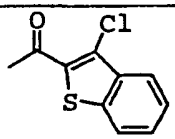
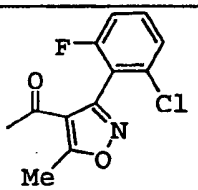
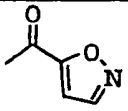
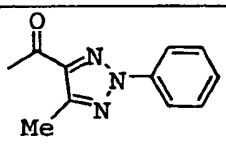
TABLE 2 Examples 55a-bi

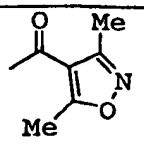
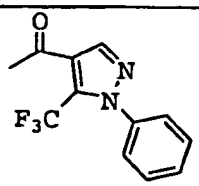
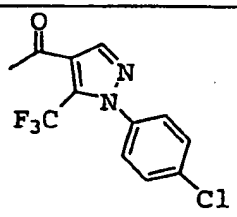
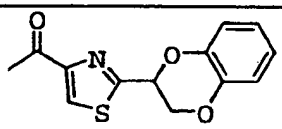
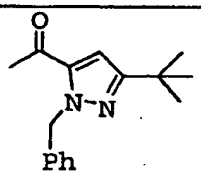
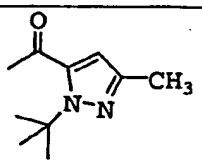
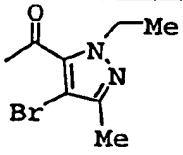
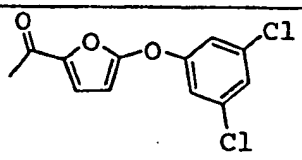
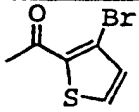
Ex.#	R =	Calc Mass	Calc M+H	Found M+H
55a		359.616	360.616	360
55b		393.633	394.633	394

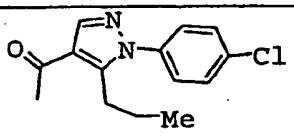
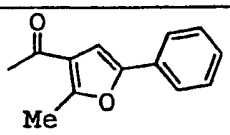
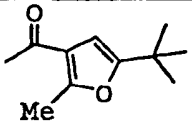
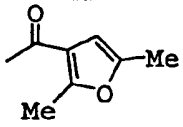
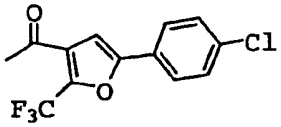
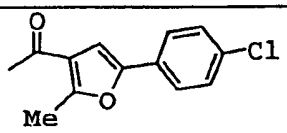
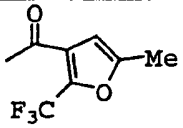
55c		369.611	370.611	370
55d		492.121	493.121	491
55e		487.702	488.702	488
55f		378.579	379.579	401 M+Na
55g		378.579	379.579	379
55h		437.729	438.729	438
55i		429.666	430.666	430
55j		437.565	438.565	438
55k		422.459	423.459	422
55l		422.459	423.459	422
55m		413.62	414.62	414
55n		403.628	404.628	404

55o		403.63	404.63	404
55p		455.66	456.66	456
55q		343.53	344.53	344
55r		354	355	355
55s		354	355	355
55t		506.752	507.752	507
55u		397.577	398.577	398
55v		405.605	406.605	406
55w		563.631	564.631	564
55x		381.622	382.622	382

55y		443.693	444.693	444
55z		381.622	382.622	382
55aa		550.825	551.825	573
55ab		418.039	419.039	418
55ac		353.568	354.568	354
55ad		469.087	470.087	469
55ae		457.62	458.62	456
55af		419.648	420.648	420
55ag		446.674	447.674	496 M+Na
55ah		439.682	440.682	440
55ai		479.703	480.703	502 M+Na

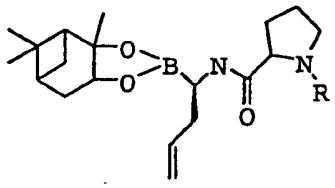
55aj		439.682	440.682	440
55ak		463.745	464.745	486 M+Na
55al		415.66	416.66	438 M+Na
55am		359.597	360.597	382 M+Na
55an		409.656	410.656	410
55ao		503.532	504.532	504
55ap		444.102	445.102	466 M+Na
55aq		487.077	488.077	509 M+Na
55ar		344.518	345.518	367 M+Na
55as		434.646	435.646	435

55at		372.571	373.571	395 M+Na
55au		487.628	488.628	488
55av		522.073	523.073	544 M+Na
55aw		494.718	495.718	495
55ax		489.765	490.765	489
55ay		413.668	414.668	414
55az		464.51	465.51	465
55ba		504.517	505.517	504
55bb		438.493	439.493	440

55bc		496.157	497.157	496
55bd		433.654	434.654	434
55be		413.664	414.664	414
55bf		371.583	372.583	372
55bg		522.069	523.069	644 M+Na
55bh		468.099	469.099	469
55bi		425.554	426.554	426

Example 56

Preparation of H-Pro-boroAlg-pinanediol•trifluoroacetate and RCO-Pro-boroAlg-$C_{10}H_{16}$ and RSO_2-Pro-boroAlg-$C_{10}H_{16}$. R is defined in Example 55.

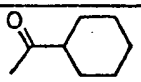
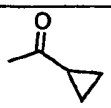
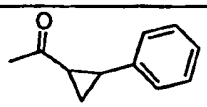
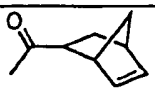
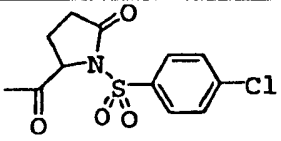
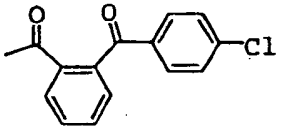
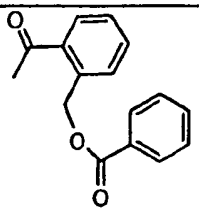
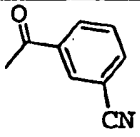
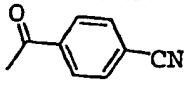
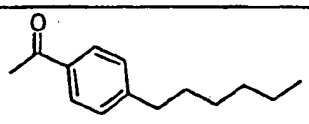
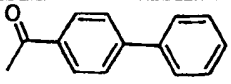


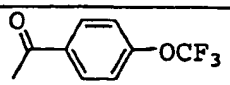
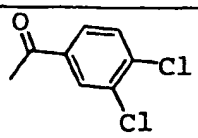
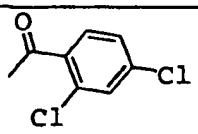
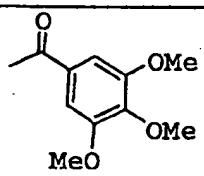
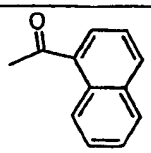
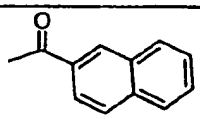
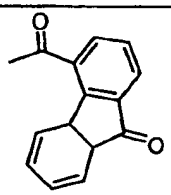
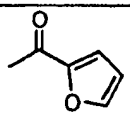
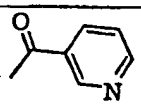
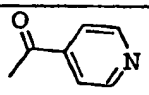
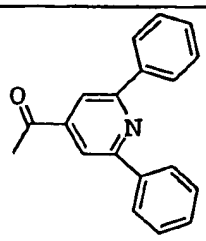
H-Pro-boroAlg-$C_{10}H_{16}$•TFA. Boc-Pro-boroAlg-pinanediol (from Example 6, 1.0 g, 2.2 mmol) was dissolved in 10 mL of

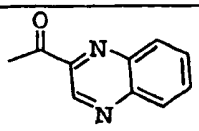
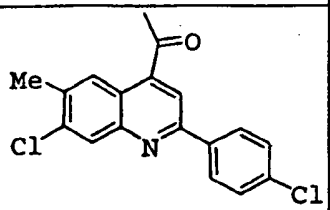
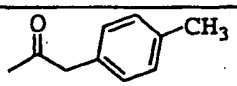
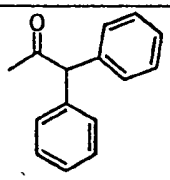
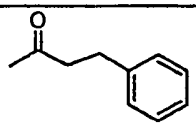
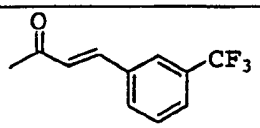
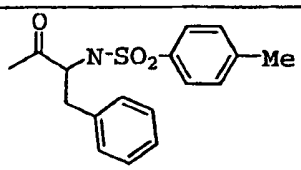
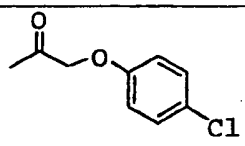
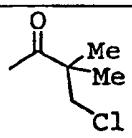
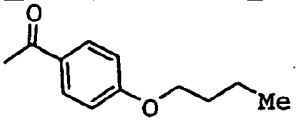
1:1 TFA: CH_2Cl_2 and stirred at room temperature for 1 h. Solvent was removed by evaporation *in vacuo* and the residue was dried over P_2O_5 overnight to yield a yellow-green oil (0.76g, 2.0 mmol, 91%). ESI/MS calculated for $C_{19}H_{31}N_2O_3B$ +H: 347.2. Found: 347.4.

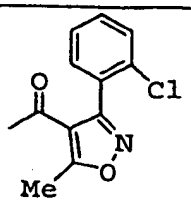
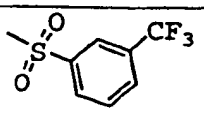
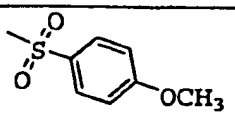
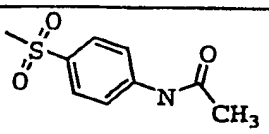
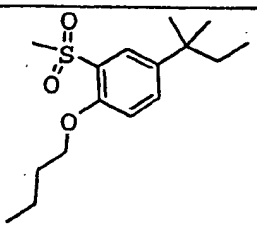
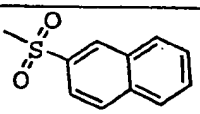
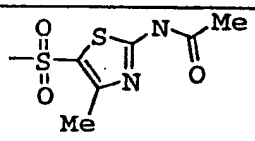
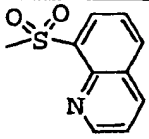
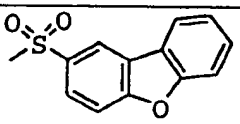
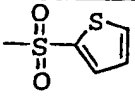
R-CO- and RSO_2-Pro-boroAlg- $C_{10}H_{16}$. R-CO-Cl and R-SO_2-Cl were allowed to react with H-Pro-boroAlg-$C_{10}H_{16}$ by the procedure described for the preparation of N-Cyclohexanoyl-boroAlg-$C_{10}H_{16}$ in Example 55. Compounds are shown it Table 3.

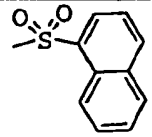
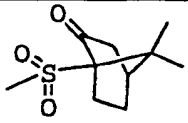
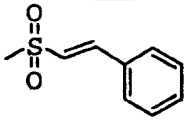
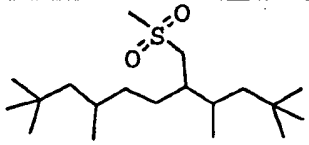
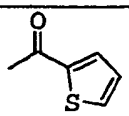
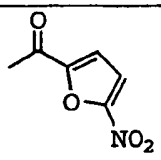
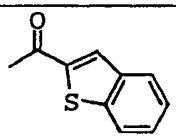
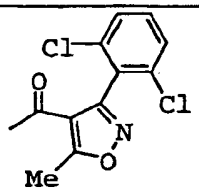
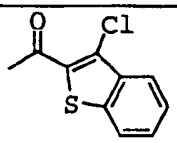
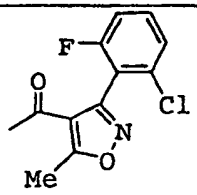
TABLE 3 Examples 56a-bs

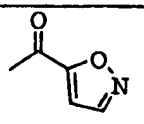
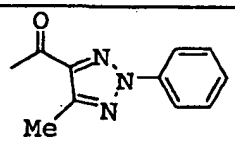
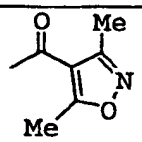
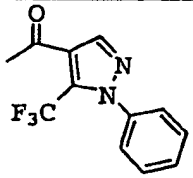
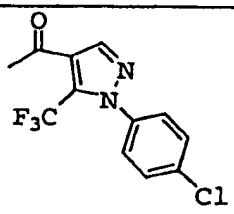
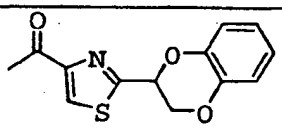
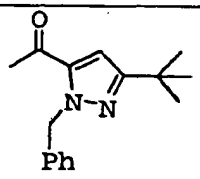
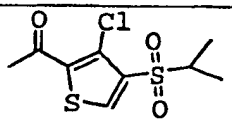
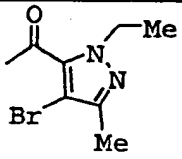
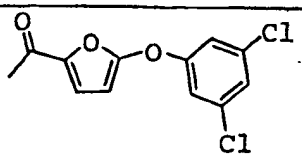
Ex.#	R =	Calc Mass	Calc M+H	Found M+H
56a		456.1	457.1	457
56b		414.0	415.0	415
56c		490.1	491.1	491
56d		466.1	467.1	467
56e		611.2	612.2	612
56f		588.6	589.6	611 M+Na
56g		584.2	585.2	585
56h		475.1	476.1	476
56I		475.1	476.1	498 M+Na
56j		534.2	535.2	535
56k		526.2	527.2	527

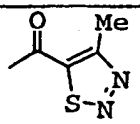
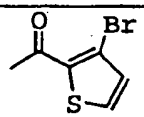
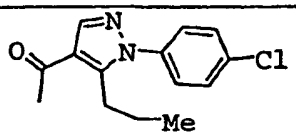
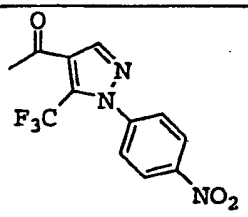
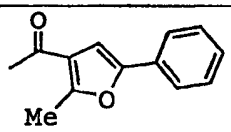
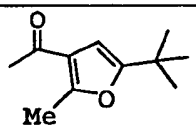
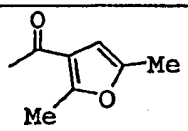
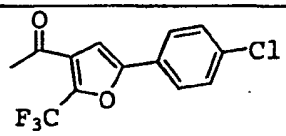
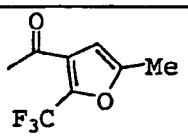
56l		534.1	535.1	535
56m		519.0	520.0	541 M+Na
56n		519.0	520.0	519
56o		540.1	541.1	541
56p		500.1	501.1	501
56q		500.1	501.1	501
56r		552.2	553.2	553
56s		440.0	441.0	441
56t		450.5	451.5	452
56u		450.5	451.5	474 M+Na
56v		603.3	504.3	626 M+Na

56w		502.1	503.1	503
56x		660.1	661.1	682 M+Na
56y		478.1	479.1	479
56z		540.2	541.2	541
56aa		478.1	479.1	479
56ab		544.1	545.1	545
56ac		647.3	648.3	648
56ad		514.5	515.5	515
56ae		464.5	465.5	465
56af		522.2	523.2	523

56ag		565.6	566.6	566
56ah		554.1	555.1	555
56ai		516.1	517.1	539 M+Na
56aj		543.2	544.2	566 M+Na
56ak		628.4	629.4	629
56al		536.2	537.2	559 M+Na
56am		564.2	565.2	565
56an		537.2	538.2	538
56ao		576.2	577.2	599 M+Na
56ap		492.2	493.2	515 M+Na

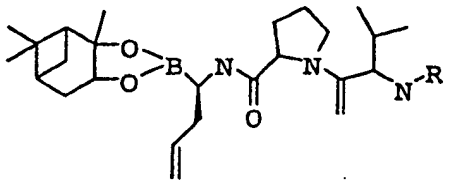
56aq		536.2	537.2	559 M+Na
56ar		560.2	561.2	561
56as		512.2	513.2	535 M+Na
56at		662.5	663.5	663
56au		456.1	457.1	457
56av		485.0	486.0	508 M+Na
56aw		506.2	507.2	507
56ax		600.0	601.0	600
56ay		540.6	541.6	541
56az		583.6	584.6	584

56ba		441.0	442.0	442
56bb		531.1	532.1	554 M+Na
56bc		469.1	470.1	470
56bd		584.1	585.1	585
56be		618.6	619.6	619
56bf		591.2	592.2	592
56bg		586.3	587.3	587
56bh		596.7	597.7	597
56bi		561.0	562.0	561
56bj		601.0	602.0	601

56bk		472.1	473.1	495 M+Na
56bl		535.0	536.0	557 M+Na
56bm		592.7	593.7	593
56bn		629.1	630.1	630
56bo		530.2	531.2	531
56bp		510.2	511.2	511
56bq		468.1	469.1	469
56br		618.6	619.6	641 M+Na
56bs		522.1	523.1	523

Example 57

Preparation of H-Val-Pro-boroAlg-$C_{10}H_{16}$•trifluoroacetate and R-CO- and R-SO_2-Val-Pro-boroAlg-$C_{10}H_{16}$.



Boc-Val-Pro-OH. Boc-Val-Pro-OBzl (from Example 9, 7.8 g, 19.3 mmol) was dissolved in 100 mL methanol containing 1% acetic acid. Pearlman's catalyst, $Pd(OH)_2$, (100 mg) was added and the flask was placed on the Parr hydrogenation apparatus. After hydrogen consumption was complete, the catalyst was removed by filtration through a celite pad. The filtrate was condensed *in* vacuo to yield a yellow oil (6.1 g, 100%). ESI/MS calculated for $C_{15}H_{26}N_2O_5$ +H: 315.2. Found: 315.3.

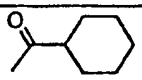
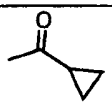
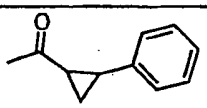
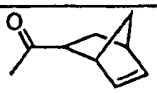
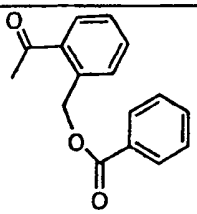
Boc-Val-Pro- boroAlg pinanediol. Boc-Val-Pro-OH (1.3 g, 4.1 mmol) was dissolved in DMF (14 mL) and chilled to -20°C in a carbon tetrachloride/dry ice bath. Isobutyl chloroformate (0.54 mL, 4.1 mmol) and NMM (0.46 mL, 4.1 mmol) were added. After 5 minutes, the mixed anhydride preparation was added to H-boroAlg-$C_{10}H_{16}$•HCl (Example 1, 1.2 g, 4.1 mmol) dissolved in DMF (9 mL) also cooled to -20°C. Additional cold DMF (~5 mL) was used to aid in the transfer. Triethylamine (0.58 mL, 4.1 mmol) was added and the reaction mixture was allowed to come to room temperature and stir overnight. The mixture was filtered, and evaporated *in vacuo*. The residue was dissolved in ethyl acetate, washed with 0.2N HCl, 5% $NaHCO_3$, and saturated NaCl solutions. The organic phase was dried over sodium sulfate, filtered, and evaporated to yield an oil which was further purified by silica gel chromatography (hexane: ethyl acetate). A step wise gradient for 100%

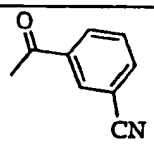
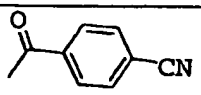
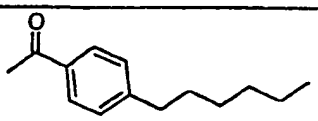
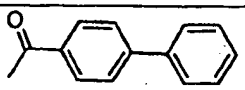
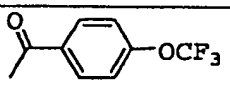
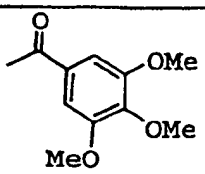
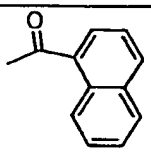
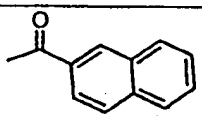
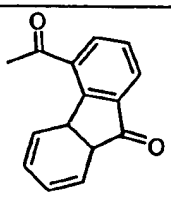
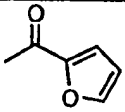
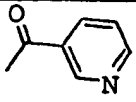
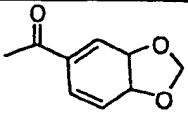
hexane to 100% ethyl acetate was run. The desired product was eluted with 100% ethyl acetate. TLC ran in ethyl acetate indicated a single spot at R_F 0.41. Solvent was removed by evaporation *in vacuo* to yield a foam (1.27g, 2.3 mmol, 57%). ESI/MS calculated for $C_{29}H_{48}N_3O_6B$+H: 546.4. Found: 546.3.

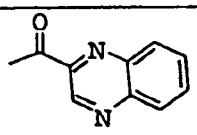
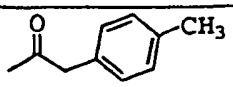
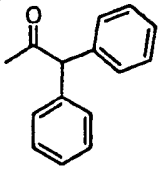
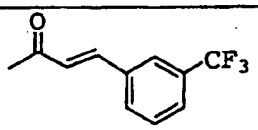
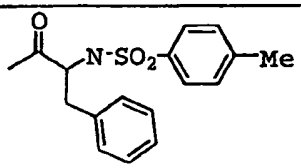
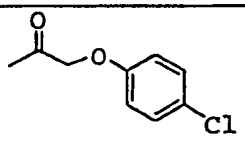
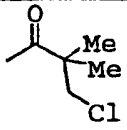
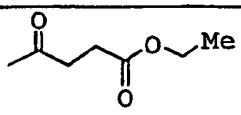
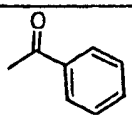
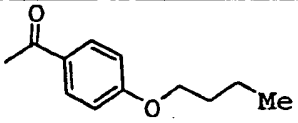
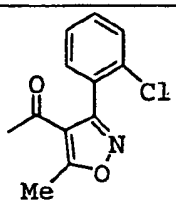
H-Val-Pro-boroAlg pinanediol ester•trifluoroacetate. The Boc peptide (100 mg, 0.18 mmol) was dissolved in 2 mL of 1:1 TFA: CH_2Cl_2 and stirred at room temperature for 2 hours. The reaction mixture was evaporated *in vacuo* and stored under vacuum with P_2O_5 overnight to yielded a yellow solid (80 mg, 0.17 mmol, 94%). ESI/MS calculated for $C_{24}H_{40}N_3O_4B$ +H: 446.3. Found: 446.3.

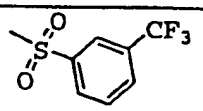
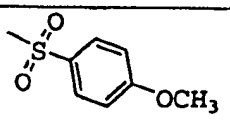
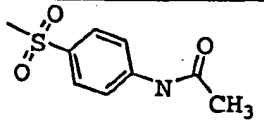
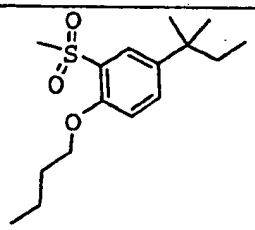
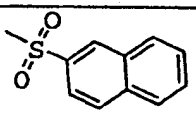
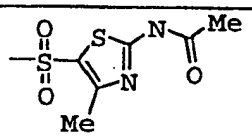
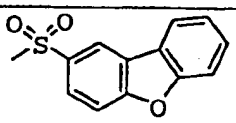
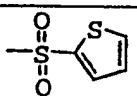
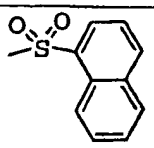
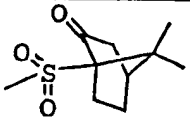
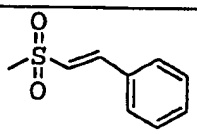
R-CO- and RSO_2-Val-Pro-boroAlg-$C_{10}H_{16}$. R-CO-Cl and R-SO_2-Cl were allowed to react with H-Pro-boroAlg-$C_{10}H_{16}$ by the procedure described for the preparation of N-Cyclohexanoyl-boroAlg-$C_{10}H_{16}$ in Example 55. Compounds are shown it Table 4.

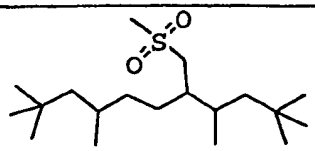
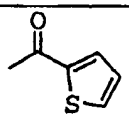
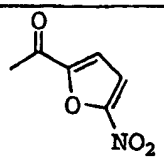
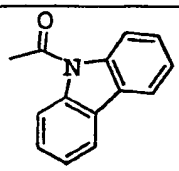
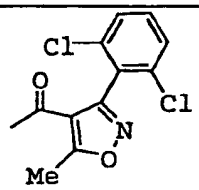
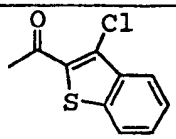
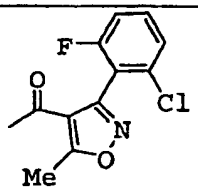
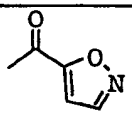
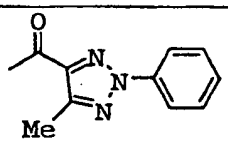
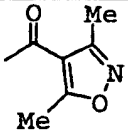
TABLE 4. Examples 57a-bj

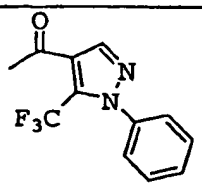
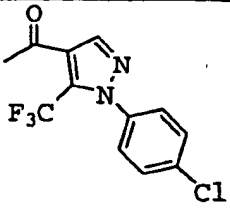
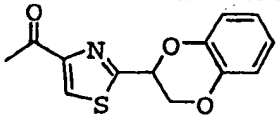
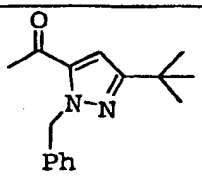
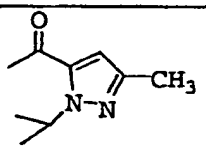
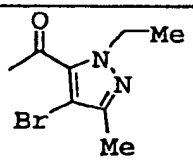
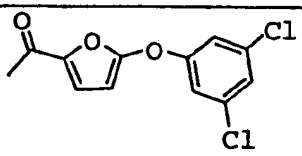
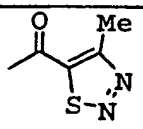
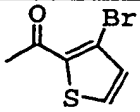
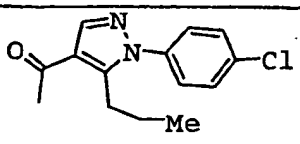
Ex.#	R =	Calc Mass	Calc M+H	Found M+H
57a		555.1	556.1	578 M+Na
57b		513.0	514.0	536 M+Na
57c		589.1	590.1	612 M+Na
57d		565.1	566.1	588 M+Na
57e		683.2	684.2	706 M+Na

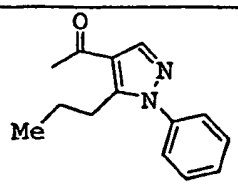
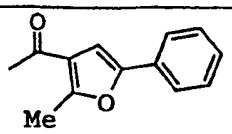
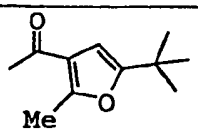
57f		574.1	575.1	597 M+Na
57g		574.1	575.1	597 M+Na
57h		633.2	634.2	656 M+Na
57i		625.2	626.2	648 M+Na
57j		633.1	634.1	656 M+Na
57k		639.1	640.1	640
57l		599.1	600.1	622 M+Na
57m		599.1	600.1	622 M+Na
57n		651.2	652.2	652
57o		539.0	540.0	540
57p		549.5	550.5	573 M+Na
57q		593.1	594.1	616 M+Na

57r		601.1	602.1	624 M+Na
57s		577.1	578.1	600 M+Na
57t		577.1	578.1	600 M+Na
57u		643.1	644.1	666 M+Na
57v		746.3	747.3	769 M+Na
57w		613.5	614.5	636 M+Na
57x		563.5	564.5	586 M+Na
57y		573.1	574.1	596 M+Na
57z		549.1	550.1	572 M+Na
57aa		621.2	622.2	644 M+Na
57ab		664.6	665.6	687 M+Na

57ac		653.1	654.1	676 M+Na
57ad		615.1	616.1	638 M+Na
57ae		642.2	643.2	665 M+Na
57af		727.4	728.4	750 M+Na
57ag		635.2	636.2	
57ah		663.2	664.2	686 M+Na
57ai		675.2	676.2	698 M+Na
57aj		591.2	592.2	614 M+Na
57ak		635.2	636.2	658 M+Na
57al		659.2	660.2	682 M+Na
57am		611.2	612.2	634 M+Na

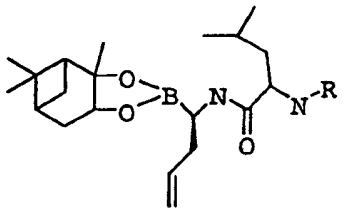
57an		761.5	762.5	784 M+Na
57ao		555.1	556.1	578 M+Na
57ap		584.0	585.0	608 M+Na
57aq		605.2	606.2	629 M+Na
57ar		669.0	700.0	723 M+Na
57as		639.6	640.6	663 M+Na
57at		682.6	683.6	706 M+Na
57au		540.0	541.0	564 M+Na
57av		630.1	631.1	653 M+Na
57aw		568.1	569.1	591 M+Na

57ax		683.1	684.1	706 M+Na
57ay		717.6	718.6	740 M+Na
57az		690.2	691.2	713 M+Na
57ba		685.3	686.3	708 M+Na
57bb		609.2	610.2	632 M+Na
57bc		660.0	661.0	684 M+Na
57bd		700.0	701.0	722 M+Na
57be		571.1	572.1	594 M+Na
57bf		634.0	635.0	656 M+Na
57bg		691.7	692.7	714 M+Na

57bh		657.2	658.2	682 M+Na
57bi		629.2	630.2	652 M+Na
57bj		609.2	610.2	632 M+Na

Example 58

Preparation of H-Leu-boroAlg-pinanediol ester•HCl and R-CO- and R-SO_2-Leu-boroAlg-$C_{10}H_{16}$.



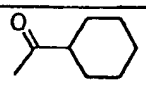
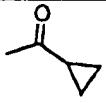
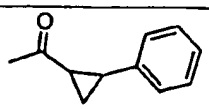
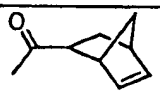
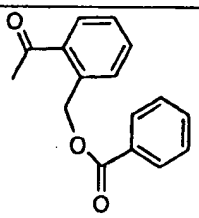
Boc-Leu-boroAlg-pinanediol ester. Boc-Leu-OH (1.6 g, 5.0 mmol) was dissolved in chloroform (15 mL) and chilled to -20°C in a carbon tetrachloride/dry ice bath. Isobutyl chloroformate (0.65 mL, 5.0 mmol) and NMM (0.55 mL, 5.0 mmol) were added and, after 5 minutes, the mixture was added to H-boroAlg-pinanediol•hydrochloride (1.4 g, 5.0 mmol) dissolved in chloroform (10 mL) and also cooled to -20°C. Cold chloroform was used to aid in the transfer. Triethylamine (0.69 mL, 5.0 mmol) was added and the reaction mixture stirred overnight gradually warming to room temperature. The mixture was filtered, and evaporated *in vacuo*. The residue was dissolved in ethyl acetate, washed with 0.2 N HCl, 5% $NaHCO_3$, and saturated aqueous

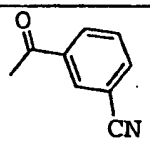
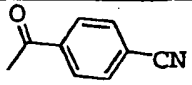
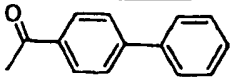
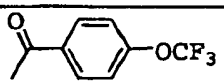
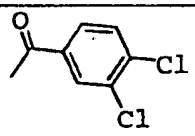
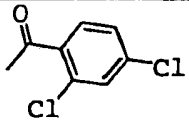
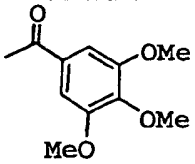
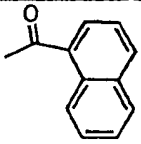
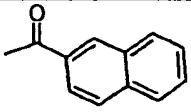
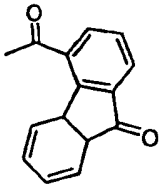
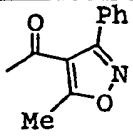
NaCl. The organic phase was dried over sodium sulfate, filtered and evaporated to yield an oil (2.0 g). It was purified by silica gel chromatography (7: 3 hexane: ethyl acetate). TLC indicated a single spot R_F 0.63 hexane/ethyl acetate (1:1). This yielded a white solid (470 mg, 1.0 mmol, 20%). ESI/MS calculated for $(C_{25}H_{43}N_2O_5B)2$ +H: 925.6. Found: 925.7.

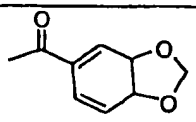
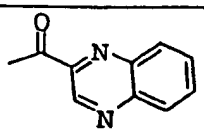
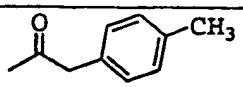
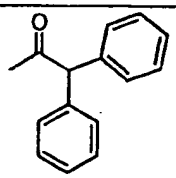
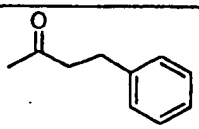
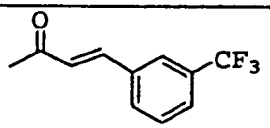
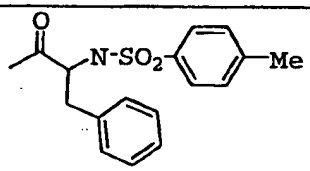
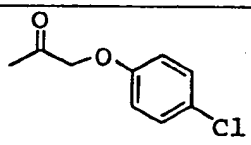
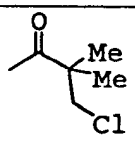
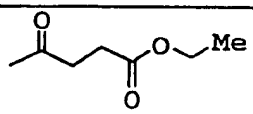
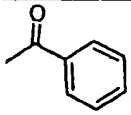
The Boc peptide (350 mg, 0.76 mmol) was dissolved in 4 N HCl in dioxane. The reaction mixture stirred at room temperature for 2 hours. It was evaporated *in vacuo* and stored over P_2O_5 overnight to yield the desired product as a yellow oil (256 mg, 0.71mmol, 95%). ESI/MS calculated for $C_{20}H_{35}N_2O_3B$ +H: 363.3. Found: 363.4.

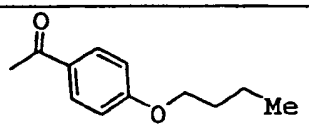
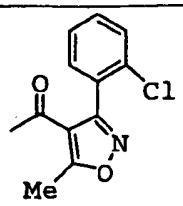
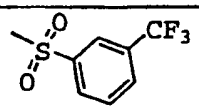
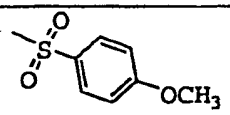
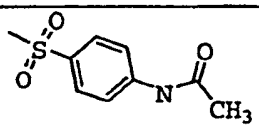
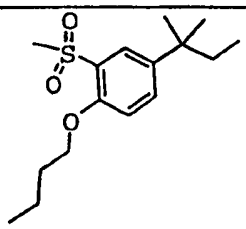
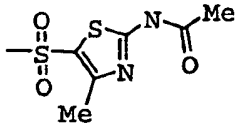
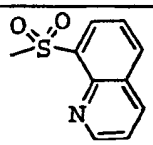
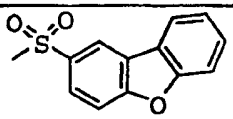
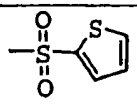
R-CO- and RSO_2-Leu-boroAlg- $C_{10}H_{16}$. R-CO-Cl and R-SO_2-Cl were allowed to react with H-Leu-boroAlg-$C_{10}H_{16}$ by the procedure described for the preparation of N-Cyclohexanoyl-boroAlg-$C_{10}H_{16}$ in Example 55. Compounds are shown in Table 5.

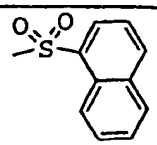
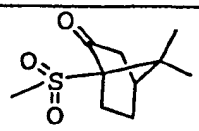
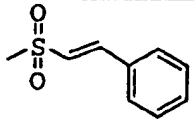
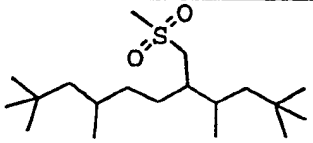
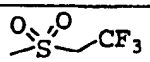
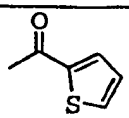
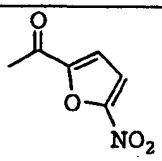
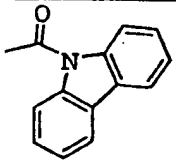
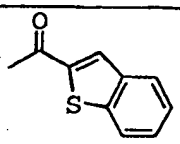
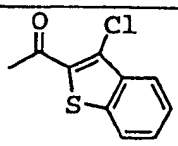
TABLE 5 Examples 58a-bq

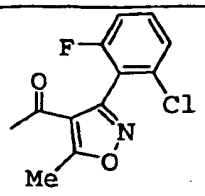
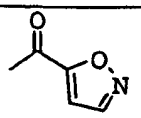
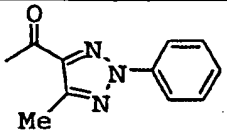
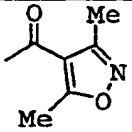
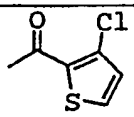
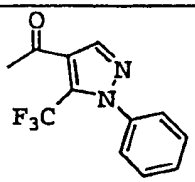
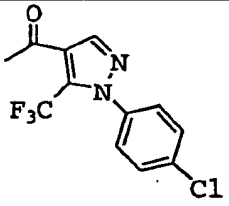
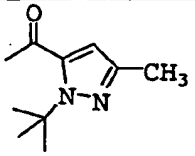
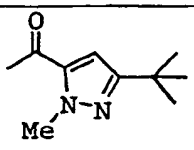
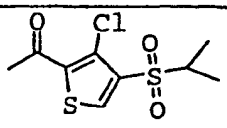
Ex.#	R =	Calc Mass	Calc M+H	Found M+H
58a		472.5	473.5	472.4
58b		430.4	431.4	431.4
58c		506.5	507.5	507.4
58d		482.5	483.5	483.4
58e		600.6	601.6	601.4

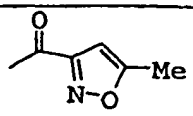
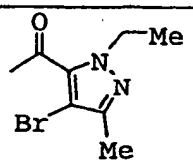
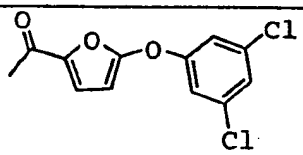
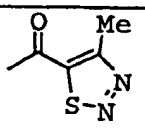
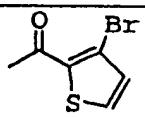
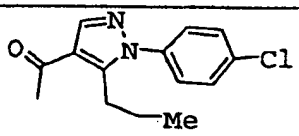
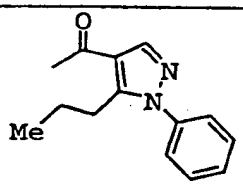
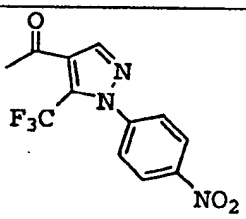
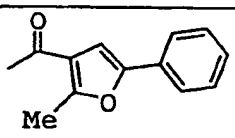
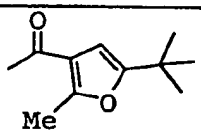
58f		491.4	492.4	492.4
58g		491.4	492.4	492.4
58h		542.5	543.5	543.4
58I		550.4	551.4	551.4
58j		534.3	535.3	535.3
58k		535.3	536.3	535.3
58l		550.6	551.6	573.4 M+Na
58m		516.5	517.5	517.4
58n		516.5	517.5	517.4
58o		456.4	457.4	457.4
58p		547.5	548.5	548.4

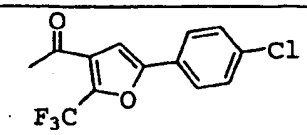
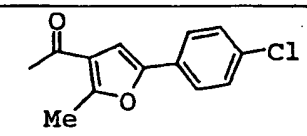
58q		510.4	511.4	511.4
58r		518.5	519.5	519.3
58s		494.5	495.5	495.4
58t		556.6	557.6	557.4
58u		494.5	495.5	495.4
58v		560.5	561.5	561.3
58w		663.7	664.7	686.4 M+Na
58x		530.9	531.9	551.3
58y		480.9	481.9	481.3
58z		490.4	491.4	491.4
58aa		466.4	467.4	467.3

58ab		538.5	539.5	539.4
58ac		581.9	582.9	582.3
58ad		570.5	571.5	571.3
58ae		552.5	553.5	555.3
58af		559.5	560.5	560.3
58ag		644.7	645.7	645.7
58ah		580.6	581.6	581.3
58ai		552.5	553.5	553.3
58aj		592.6	593.6	593.3
58ak		508.5	509.5	531.3 M+Na

58al		552.5	553.5	553.3
58am		576.6	577.6	599.4 M+Na
58an		528.5	529.5	529.3
58ao		678.9	679.9	701.5 M+Na
58ap		508.4	509.4	509.3
58aq		472.5	473.5	473.5
58ar		501.4	502.4	525.5 M+Na
58as		522.5	523.5	523.5
58at		557.0	558.0	557.4
58au		599.9	600.9	600.5

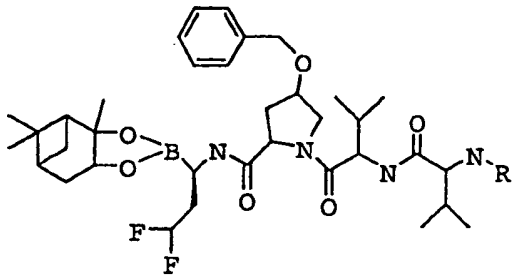
58av		457.4	458.4	458.5
58aw		547.5	548.5	548.5
58ax		485.4	486.4	486.5
58ay		506.9	507.9	507.4
58az		600.5	601.5	601.4
58ba		634.9	635.9	635.4
58bb		526.5	527.5	527.5
58bc		526.5	527.5	527.5
58bd		612.0	613.0	613.4
58be		471.4	472.4	472.4

58bf		576.4	577.4	577.3
58bg		616.4	617.4	617.3
58bh		488.5	489.5	511.4 M+Na
58bi		550.4	551.4	551.3
58bj		608.0	609.0	609.4
58bk		574.6	575.6	575.4
58bl		645.5	646.5	646.4
58bm		546.5	547.5	547.4
58bn		526.5	527.5	527.4
58bo		634.9	635.9	635.4

58bp		581.0	582.0	603.4 M+Na
58bq		538.4	539.4	539.4

Example 59

Preparation of H-Val-Val-Hyp(OBzl)- boroDfb-$C_{10}H_{16}$ and R-CO- and R-SO_2-Val-Val-Hyp(OBzl)- boroDfb-$C_{10}H_{16}$.

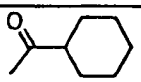
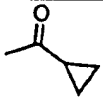
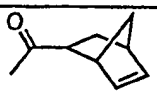
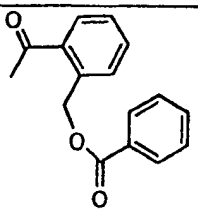
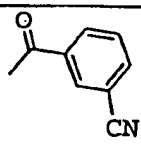
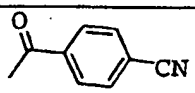
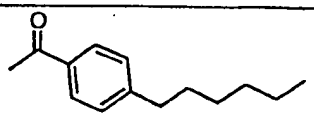
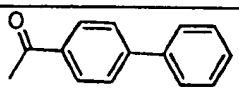
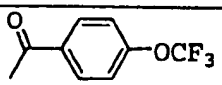
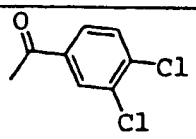
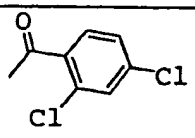


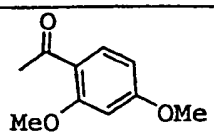
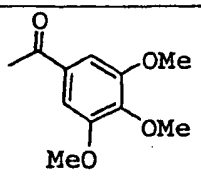
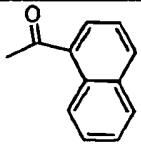
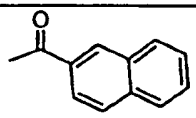
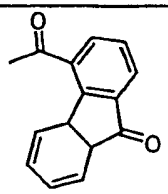
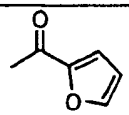
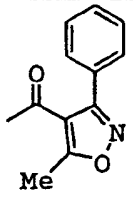
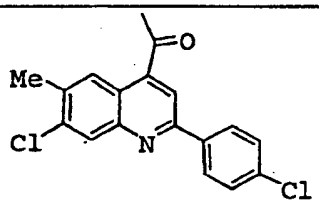
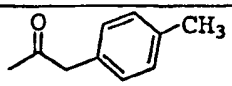
Boc-Val-Val-Hyp(OBzl)- boroDfb-$C_{10}H_{16}$ H-Hyp(OBzl)-boroDfb-$C_{10}H_{16}$ (See Example 43) was coupled to Boc-Val-Val-OH using DCC coupling following the procedure as described in Example 9.

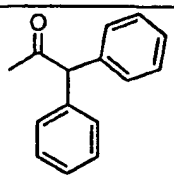
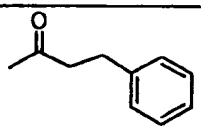
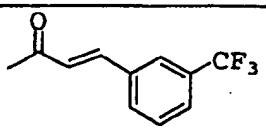
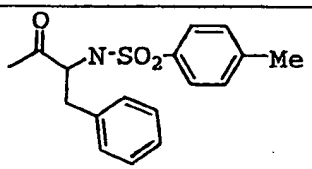
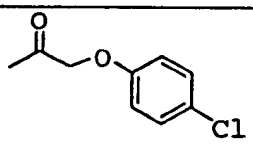
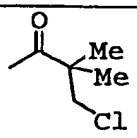
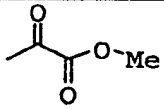
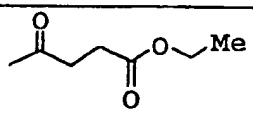
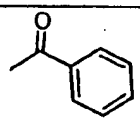
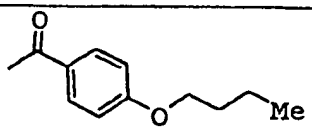
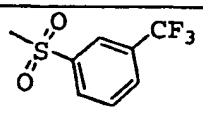
H-Val-Val-Hyp(OBzl)-boroDfb-$C_{10}H_{16}$. Boc-Val-Val-Hyp(OBzl)-boroDfb-$C_{10}H_{16}$ was deprotected using a procedure similar to that described in Example 9.

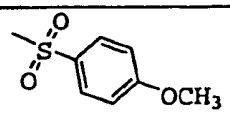
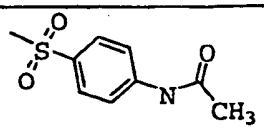
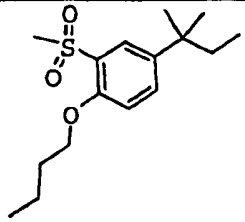
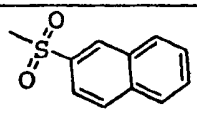
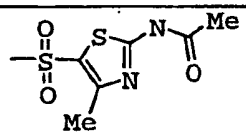
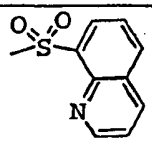
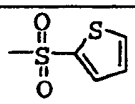
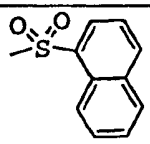
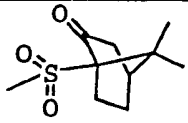
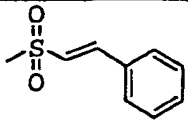
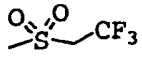
R-CO- and R-SO_2-Val-Val-Hyp(OBzl)- boroDfb-$C_{10}H_{16}$. R-CO-Cl and R-SO_2-Cl were allowed to react with H-Val-Val-Hyp(OBzl)-boroDfb-$C_{10}H_{16}$ by the procedure described for the preparation of N-Cyclohexanoyl-boroDfb-$C_{10}H_{16}$ in Example 55. Compounds are shown in Table 6.

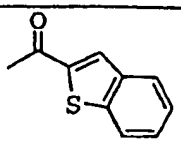
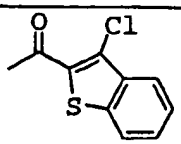
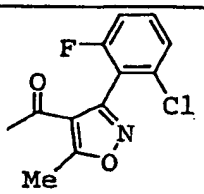
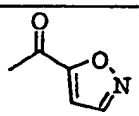
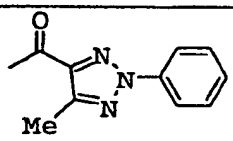
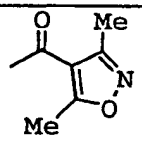
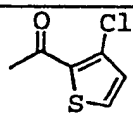
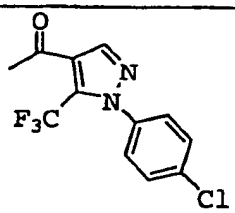
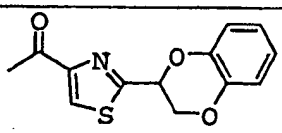
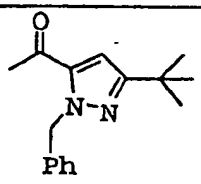
TABLE 6 Examples 59a-bj

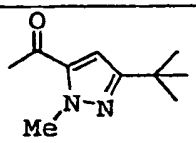
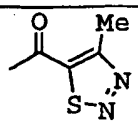
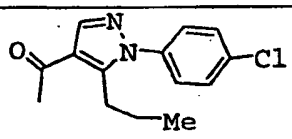
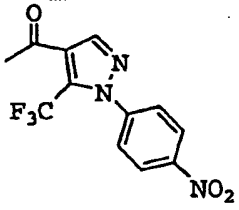
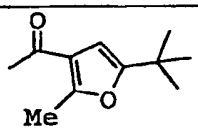
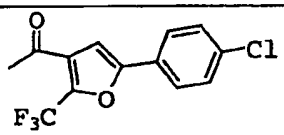
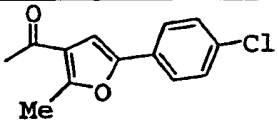
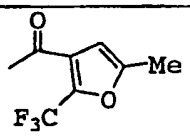
Ex.#	R =	Calc Mass	Calc M+H	Found M+H
59a		784.1	785.1	785.7
59b		742.0	743.0	743.6
59c		818.4	819.4	819.6
59d		794.1	795.1	795.6
59e		912.2	913.2	935.6 M+Na
59f		803.1	804.1	826.3 M+Na
59g		803.1	804.1	826.36 M+Na
59h		862.2	863.2	863.4
59I		854.2	855.2	855.3
59j		862.1	863.1	885.2 M+Na
59k		847.0	848.0	869.2 M+Na
59l		847.0	848.0	869.2 M+Na

59m		838.1	839.1	861.3 M+Na
59n		868.2	869.2	891.3 M+Na
59o		828.1	829.1	851.3 M+Na
59p		828.1	829.1	851.3 M+Na
59q		880.2	881.2	903.2 M+Na
59r		768.0	769.0	791.2 M+Na
59s		859.2	860.2	882.3 M+Na
59t		988.1	989.1	988.3
59u		806.1	807.1	829.3 M+Na

59v		868.2	869.2	891.3 M+Na
59w		829.1	830.1	829.3
59x		872.1	873.1	895.2 M+Na
59y		975.3	976.3	998.2 M+Na
59z		842.5	843.5	865.5 M+Na
59aa		792.5	793.5	815.5 M+Na
59ab		760.0	761.0	761.5
59ac		802.1	803.1	803.6
59ad		778.1	7779.1	779.5
59ae		850.2	851.2	851.6
59af		882.1	883.1	883.5

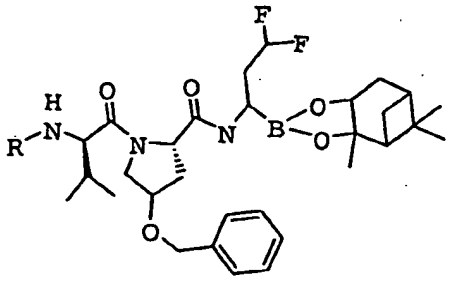
59ag		844.2	845.2	845.5
59ah		871.2	872.2	872.6
59ai		956.4	957.4	957.7
59aj		864.2	865.2	887.5 M+Na
59ak		892.2	893.2	893.5
59al		865.2	866.2	866.5
59am		820.2	821.2	843.5 M+Na
59an		864.2	865.2	887.5 M+Na
59ao		888.3	889.3	911.6 M+Na
59ap		840.2	841.2	863.5 M+Na
59aq		820.1	821.1	843.5 M+Na

59ar		834.2	835.2	875.6 M+Na
59as		868.6	869.6	891.5 M+Na
59at		911.6	912.6	934.5 M+Na
59au		769.0	770.0	792.5 M+Na
59av		859.1	860.1	882.6 M+Na
59aw		797.1	798.1	798.5
59ax		818.5	819.5	841.4 M+Na
59ay		946.6	947.6	969.5 M+Na
59az		919.2	920.2	942.5 M+Na
59ba		914.3	915.3	937.6 M+Na

59bb		924.7	925.7	947.4 M+Na
59bc		800.1	801.1	823.6 M+Na
59bd		886.2	887.2	887.7
59be		957.1	958.1	980.6 M+Na
59bf		838.2	839.2	861.7 M+Na
59bg		946.6	947.6	947.6
59bh		892.6	893.6	915.6 M+Na
59bi		850.1	851.1	873.6 M+Na

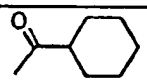
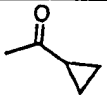
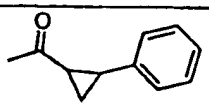
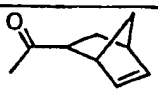
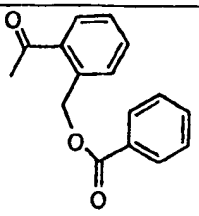
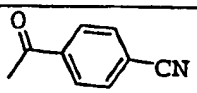
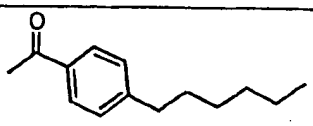
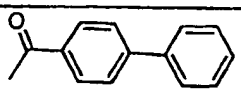
Example 60

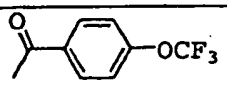
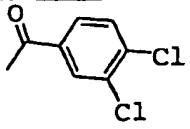
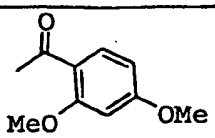
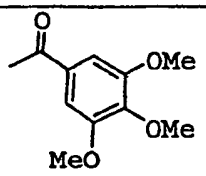
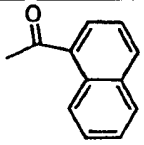
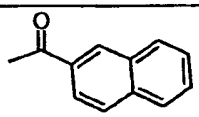
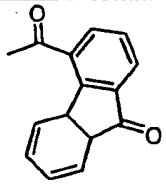
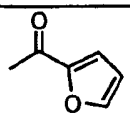
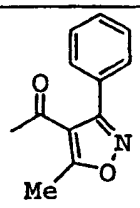
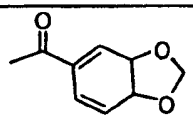
Preparation of R-CO-Val-Val-Hyp(OBzl)-boroDfb-$C_{10}H_{16}$ and R-SO_2-Val-Val-Hyp(OBzl)-boroDfb-$C_{10}H_{16}$.

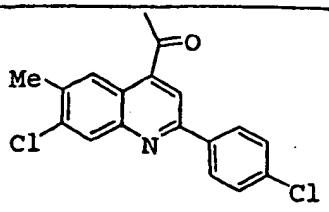
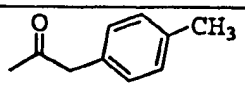
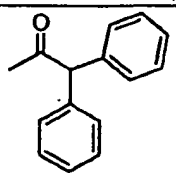
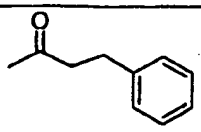
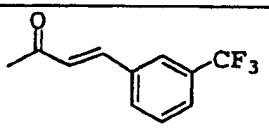
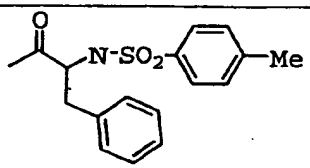
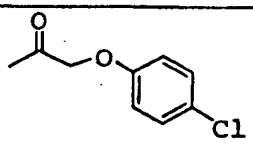
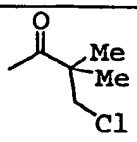
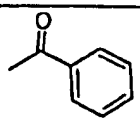
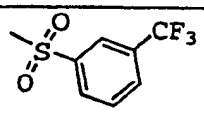
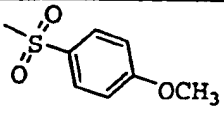


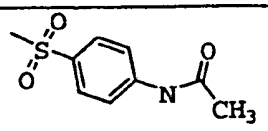
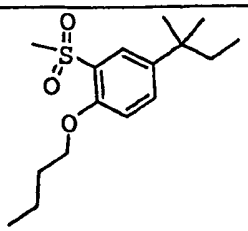
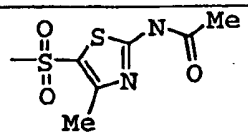
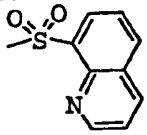
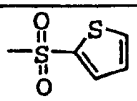
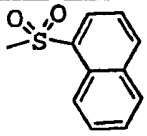
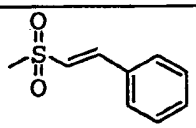
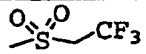
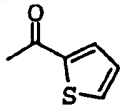
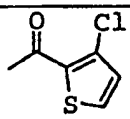
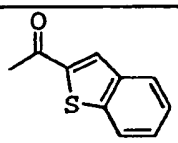
Compounds in Table 7 were prepared using the procedures disclosed herein.

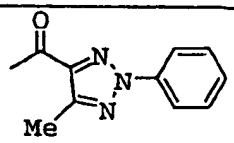
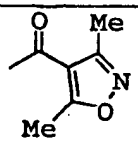
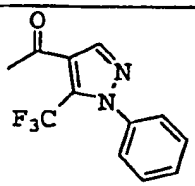
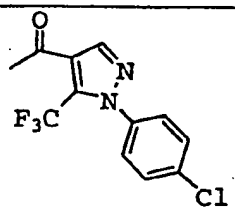
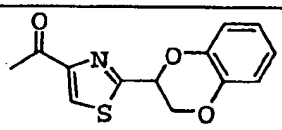
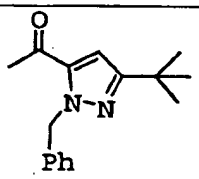
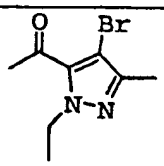
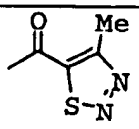
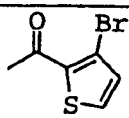
TABLE 7 Examples 60a-60bc

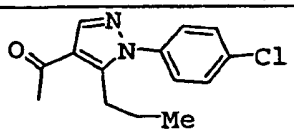
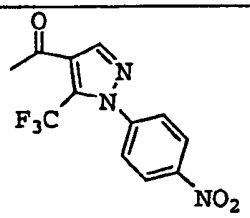
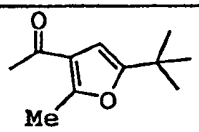
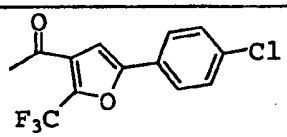
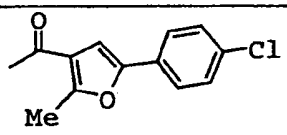
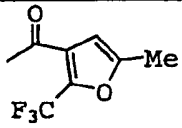
Ex.#	R =	Calc Mass	Calc M+H	Found M+H
60a		685.6	686.6	686.7
60b		643.5	644.5	644.6
60c		719.9	720.9	720.7
60d		695.6	696.6	696.7
60e		813.7	812.7 M-H	812.6 M-H
60f		704.6	703.6 M-H	703.6 M-H
60g		763.7	762.7 M-H	762.7 M-H
60h		755.7	754.7 M-H	754.6 M-H

60I		763.6	764.6	764.6
60j		748.5	772.5 M+Na	773.5 M+Na
60k		739.6	740.6	740.7
60l		769.7	768.7	768.6
60m		729.6	728.6	728.6
60n		729.6	728.6	728.6
60o		781.7	780.7 M-H	780.6 M-H
60p		669.5	670.5	670.6
60q		760.7	759.7 M-H	759.6 M-H
60r		723.6	722.6 M-H	722.5 M-H

60s		731.6	732.6	732.6
60t		707.6	708.6	708.7
60u		769.7	770.7	770.7
60v		707.6	708.6	708.7
60w		773.6	772.6 M-H	772.5 M-H
60x		876.8	875.8 M-H	875.6 M-H
60y		744.0	743.0 M-H	743.5 M-H
60z		694.0	693.0 M-H	692.6 M-H
60aa		679.6	678.6 M-H	678.6 M-H
60ab		783.6	782.6 M-H	782.4 M-H
60ac		745.7	744.7 M-H	744.5 M-H

60ad		772.7	771.7 M-H	771.5 M-H
60ae		857.9	856.9 M-H	856.6 M-H
60af		793.7	794.7	764.5
60ag		766.7	765.7 M-H	765.4 M-H
60ah		721.7	720.7 M-H	720.4 M-H
60ai		765.7	764.7 M-H	764.4 M-H
60aj		741.7	742.7	742.5
60ak		721.6	720.6 M-H	720.4 M-H
60al		685.6	684.6 M-H	684.4 M-H
60am		714.5	713.5 M-H	713.4 M-H
60an		735.7	734.7 M-H	734.4 M-H

60ao		760.6	759.6 M-H	759.4 M-H
60ap		698.6	699.6	699.5
60aq		813.6	812.6 M-H	812.4 M-H
60ar		848.1	847.1 M-H	846.4 M-H
60as		820.7	819.7 M-H 844.7 M+Na	819.4 M-H 844.4 M+Na
60at		815.8	814.8 M-H	814.5 M-H
60au		790.5	814.5 M+Na	814.4 M+Na
60av		701.6	700.6 M-H	700.4 M-H
60aw		764.5	763.5 M-H	763.2 M-H

60ax		787.7	786.7 M-H 811.7 M+Na	811.5 M+Na 786.4 M-H
60ay		858.6	857.6	857.4
60az		739.7	738.7	738.4
60ba		848.1	847.1	847.4
60bb		794.1	793.1	793.4
60bc		751.6	750.6	750.4

UTILITY

The compounds of the present invention have therapeutic utility in the cure and prevention of hepatitis C virus infections, as demonstrated by the assays described below. A compound is considered active in the in vitro assay described below as an inhibitor of HCV protease if it has an IC_{50} value or a K_i value of less than about 60 micromolar; preferably less than about 20 micromolar; more preferably less than about 1 micromolar; most preferably less than about 0.10 micromolar. Compounds of the invention have been shown to have an IC_{50} value of less

than about 60 micromolar for inhibition of the NS3 protease.

Biological Activity

Expression and Purification of NS3 Protease

The plasmid cf1SODp600, containing the complete coding region of HCV NS3 protease, genotype 1a, was obtained from ATCC (database accession: DNA Seq. Acc. M62321, originally deposited by Chiron Corporation). PCR primers were designed that allow amplification of the DNA fragment encoding the NS3 protease catalytic domain (amino acids 1 to 192) as well as its two N-terminal fusions, a 5 amino acid leader sequence MGAQH (serving as a expression tag) and a 15 amino acid His tag MRGSHHHHHHMGAQH. The NS3 protease constructs were cloned in the bacterial expression vector under the control of the T7 promoter and transformed in *E. coli* BL 21 (DE3) cells. Expression of the NS3 protease was obtained by addition of 1 mM IPTG and cells were growing for additional 3 h at 25°C. The NS3 protease constructs have several fold difference in expression level, but exhibit the same level of solubility and enzyme specific activity. A typical 10 L fermentation yielded approximately 200 g of wet cell paste. The cell paste was stored at -80°C. The NS3 protease was purified based on published procedures (Steinkuhler C. et al. *Journal of Virology* 70, 6694-6700, 1996 and Steinkuhler C. et al. *Journal of Biological Chemistry* 271, 6367-6373, 1996.) with some modifications. Briefly, the cells were resuspended in lysis buffer (10 ml/g) containing PBS buffer (20 mM sodium phosphate, pH 7.4, 140 mM NaCl), 50% glycerol, 10 mM DTT, 2% CHAPS and 1mM PMSF. Cell lysis was performed with use of microfluidizer. After homogenizing, DNase was added to a final concentration 70 U/ml and cell lysate was incubated at 4°C for 20 min. After centrifugation at 18,000 rpm for 30 min at 4°C supernatant was applied on SP Sepharose column (Pharmacia), previously equilibrated at a flow rate 3 ml/min in buffer A (PBS buffer, 10% glycerol, 3 mM DTT).

The column was extensively washed with buffer A and the protease was eluted by applying 25 column volumes of a linear 0.14 - 1.0 M NaCl gradient. NS3 containing fractions were pooled and concentrated on an Amicon stirred ultrafiltration cell using a YM-10 membrane. The enzyme was further purified on 26/60 Superdex 75 column (Pharmacia), equilibrated in buffer A. The sample was loaded at a flow rate 1 ml/min, the column was then washed with a buffer A at a flow rate 2 ml/min. Finally, the NS3 protease containing fractions were applied on Mono S 10/10 column (Pharmacia) equilibrated in 50 mM Tris.HCl buffer, pH 7.5, 10% glycerol and 1 mM DTT and operating at flow rate 2 ml/min. Enzyme was eluted by applying 20 column volumes of a linear 0.1 - 0.5 M NaCl gradient. Based on SDS-PAGE analysis as well as HPLC analysis and active site titration, the purity of the HCV NS3 1a protease was greater than 95%. The enzyme was stored at -70°C and diluted just prior to use.

Enzyme Assays

Concentrations of protease were determined in the absence of NS4a by using the peptide ester substrate Ac-DED(Edans)-EEAbuψ[COO]ASK(Dabcyl)-NH_2 (Taliani et al. *Anal. Biochem.* 240, 60-67, 1996.) and the inhibitor, H-Asp-Glu-Val-Val-Pro-boroAlg-OH (Example 10), and by using tight binding reaction conditions (Bieth, *Methods Enzymol.* 248, 59-85, 1995). Best data was obtained for an enzyme level of 50 nM. Alternately, protease (63 µg/ml) was allowed to react with 3 µM NS4a, 0.10 mM Ac-Glu-Glu-Ala-Cys-*p*NA, and varying level of Example 10, (0-6 µM). Concentrations of protease were determined from linear plots of Activity vs. Concentration of Example 10. Molar concentrations of proteases were determined from the x-intercept.

K_m values were determined measuring the rate of hydrolysis of the ester substrate over a range of

concentrations from 5.0 to 100 μM in the presence of 3 μM KKNS4a (KKGSVVIVGRIVLSGKPAIIPKK). Assay were run at 25°C, by incubating ~1 nM enzyme with NS4a for 5 min in 148 μl of buffer (50 mM Tri buffer, pH 7.0, 50% glycerol, 2% Chaps, and 5.0 mM DTT. Substrate (2.0 μl) in buffer was added and the reaction was allowed to proceed for 15 min. Reactions were quenched by adding 3.0 μL of 10% TFA, and the levels of hydrolysis were determined by HPLC. Aliquots (50 μL) were injected on the HPLC and linear gradients from 90% water, 10% acetonitrile and 0.10 % TFA to 10% water, 90% acetonitrile and 0.10% TFA were run at a flow rate of 1.0 mL/min over a period of 30 min. HPLCs were run on a HP1090 using a Rainin 4.6 x 250 mm C18 column (cat # 83-201-C) fluorescent detection using 350 and 500 nm as excitation and emission wavelengths, respectively. Levels of hydrolysis were determined by measuring the area of the fluorescent peak at 5.3 min. 100% hydrolysis of a 5.0 μM sample gave an area of 7.95 ±0.38 fluorescence units.). Kinetic constants were determined from the iterative fit of the Michaelis equation to the data. Results are consistent with data from Liveweaver Burk fits and data collected for the 12.8 min peak measured at 520 nm.

Enzyme activity was also measured by measuring the increase in fluorescence with time by exciting at 355 nm and measuring emission at 495 nm using a Perkin Elmer LS 50 spectrometer. A substrate level of 5.0 μM was used for all fluorogenic assays run on the spectrometer.

Inhibitor Evaluation In vitro

Inhibitor effectiveness was determined by measuring enzyme activity both in the presence and absence of inhibitor. Velocities were fit to the equation for competitive inhibition for individual reactions of inhibitors with the enzyme using

$$v_i / v_o = [K_m (1 + I/K_i) + S] / [K_m + S].$$

The ratio v_i/v_o is equal to the ratio of the Michaelis equations for velocities measured in the presence (v_i) and absence (v_o) of inhibitor. Values of v_i / v_o were measured over a range of inhibitor concentrations with the aid of an Excel™ Spreadsheet. Reported K_i values are the average of 3-5 separate determinations. Under the conditions of this assay, the IC_{50} and K_is are comparable measures of inhibitor effectiveness.

Inhibitor Evaluation in Cell Assay

The following method was devised to assess inhibitory action of test compounds on the HCV NS3 protease in cultured cells. Because it is not possible to efficiently infect cells with hepatitis C virus, an assay was developed based on co-expression in transfected cell lines of two plasmids, one is able to direct synthesis of the NS3 protease and the other to provide a polypeptide analogous to a part of the HCV non-structural protein containing a single known peptide sequence highly susceptible to cleavage by the protease. When installed in cultured cells by one of a variety of standard methods, the substrate plasmid produces a stable polypeptide of approximately 50KD, but when the plasmid coding for the viral protease is co-expressed, the enzymatic action of the protease hydrolyzes the substrate at a unique sequence between a cysteine and a serine pair, yielding products which can be detected by antibody-based technology, eg, a western blot. Quantitation of the amounts of precursor and products can be done by scanning film auto-radiograms of the blots or direct luminescense-based emissions from the blots in a commercial scanning device. The general organization of the two plasmids is provided in Figure 1. Figure 1 describes plasmid construction maps for expression in cultured cells of HCV NS3 protease (pCMV NS3 PR) and substrate (pCMVNS5A/5B). A related assay system has been described by J. Koch and R. Bartenschlager, *Virology* 237, 78-88 (1997). The coding sequences for the NS3 protease

and the substrate were taken from genotype 1a of HCV, but other genotypes, eg 2a, may be substituted with similar results.

The DNA plasmids are introduced into cultured cells using electroporation, liposomes or other means. Synthesis of the protease and the substrate begin shortly after introduction and may be detected within a few hours by immunological means. Therefore, test compounds are added at desired concentrations to the cells within a few minutes after introducing the plasmids. The cells are then placed in a standard CO_2 incubator at 37°C, in tissue culture medium eg Dulbecco-modified MEM containing 10% bovine serum. After 6-48 hours, the cells are collected by physically scraping them from plastic dishes in which they have been growing, centrifuging them and then lysing about 10^6 of the concentrated cells in a minimal volume of buffered detergent, eg 20 µl of 1% sodium dodecyl sulfate in 0.10 M Tris-HCl, pH 6.5, containing 1% mercaptaethanol and 7% glycerol. The samples are then loaded onto a standard SDS polyacrylamide gel, the polypeptides separated by electrophoresis, and the gel contents then electroblotted onto nitrocellulose or other suitable paper support, and the substrate and products detected by decoration with specific antibodies. A typical dose-response to a test compound, Example 10, is shown in Figure 2.

Compounds which could inhibit NS3 protease effectively in in vitro experiments were found to have inhibitory activity in the cell-based assay.

DOSAGE AND FORMULATION

The HCV protease inhibitor compounds of this invention can be administered as treatment for the control or prevention of hepatitis C virus infections by any means that produces contact of the active agent with the agent's site of action, i.e., the NS3 protease, in the body of a mammal. It can be administered by any conventional means

available for use in conjunction with pharmaceuticals, either as an individual therapeutic agent or in a combination of therapeutic agents. It can be administered alone, but preferably is administered with a pharmaceutical carrier selected on the basis of the chosen route of administration and standard pharmaceutical practice.

The compounds of the present invention can be administered in such oral dosage forms as tablets, capsules (each of which includes sustained release or timed release formulations), pills, powders, granules, elixirs, tinctures, suspensions, syrups, and emulsions. Likewise, they may also be administered in intravenous (bolus or infusion), intraperitoneal, subcutaneous, or intramuscular form, all using dosage forms well known to those of ordinary skill in the pharmaceutical arts.

The dosage administered will, of course, vary depending upon known factors, such as the pharmacodynamic characteristics of the particular agent and its mode and route of administration; the age, health and weight of the recipient; the nature and extent of the symptoms; the kind of concurrent treatment; the frequency of treatment; and the effect desired. By way of general guidance, a daily dosage of active ingredient can be expected to be about 0.001 to about 1000 milligrams per kilogram of body weight, with the preferred dose being about 0.01 to about 100 mg/kg; with the more preferred dose being about 0.1 to about 30 mg/kg. Advantageously, compounds of the present invention may be administered in a single daily dose, or the total daily dosage may be administered in divided doses of two, three, or four times daily.

Dosage forms of compositions suitable for administration contain from about 1 mg to about 100 mg of active ingredient per unit. In these pharmaceutical compositions the active ingredient will ordinarily be present in an amount of about 0.5-95% by weight based on the total weight of the composition. The active ingredient can be administered orally in solid dosage forms, such as capsules, tablets and powders, or in liquid dosage forms,

such as elixirs, syrups and suspensions. It can also be administered parenterally, in sterile liquid dosage forms.

Gelatin capsules contain the active ingredient and powdered carriers, such as lactose, starch, cellulose derivatives, magnesium stearate, stearic acid, and the like. Similar diluents can be used to make compressed tablets. Both tablets and capsules can be manufactured as sustained release products to provide for continuous release of medication over a period of hours. Compressed tablets can be sugar coated or film coated to mask any unpleasant taste and protect the tablet from the atmosphere, or enteric coated for selective disintegration in the gastrointestinal tract. Liquid dosage forms for oral administration can contain coloring and flavoring to increase patient acceptance.

In general, water, a suitable oil, saline, aqueous dextrose (glucose), and related sugar solutions and glycols such as propylene glycol or polyethylene glycols are suitable carriers for parenteral solutions. Solutions for parenteral administration preferably contain a water soluble salt of the active ingredient, suitable stabilizing agents, and if necessary, buffer substances. Antioxidizing agents such as sodium bisulfite, sodium sulfite, or ascorbic acid, either alone or combined, are suitable stabilizing agents. Also used are citric acid and its salts, and sodium EDTA. In addition, parenteral solutions can contain preservatives, such as benzalkonium chloride, methyl- or propyl-paraben and chlorobutanol. Suitable pharmaceutical carriers are described in *Remington's Pharmaceutical Sciences, supra*, a standard reference text in this field.

Useful pharmaceutical dosage-forms for administration of the compounds of this invention can be illustrated as follows:

Capsules

A large number of unit capsules can be prepared by filling standard two-piece hard gelatin capsules each with

100 mg of powdered active ingredient, 150 mg of lactose, 50 mg of cellulose, and 6 mg magnesium stearic.

Soft Gelatin Capsules

A mixture of active ingredient in a digestible oil such as soybean oil, cottonseed oil or olive oil can be prepared and injected by means of a positive displacement pump into gelatin to form soft gelatin capsules containing 100 mg of the active ingredient. The capsules should then be washed and dried.

Tablets

A large number of tablets can be prepared by conventional procedures so that the dosage unit is 100 mg of active ingredient, 0.2 mg of colloidal silicon dioxide, 5 milligrams of magnesium stearate, 275 mg of microcrystalline cellulose, 11 mg of starch and 98.8 mg of lactose. Appropriate coatings may be applied to increase palatability or delay absorption.

Suspension

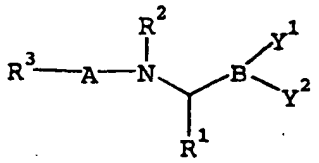
An aqueous suspension can be prepared for oral administration so that each 5 ml contain 25 mg of finely divided active ingredient, 200 mg of sodium carboxymethyl cellulose, 5 mg of sodium benzoate, 1.0 g of sorbitol solution, U.S.P., and 0.025 mg of vanillin.

Injectable

A parenteral composition suitable for administration by injection can be prepared by stirring 1.5% by weight of active ingredient in 10% by volume propylene glycol and water. The solution is sterilized by commonly used techniques.

What we claim is:

1. A method of treating Hepatitis C virus in a mammal comprising administering to said mammal in need of such treatment an effective amount of a compound of Formula (I):



(I)

or a pharmaceutically acceptable salt form thereof, wherein:

Y^1 and Y^2 are independently selected from:

a) -OH,

b) -F,

c) $-NR^{18}R^{19}$,

d) C_1-C_8 alkoxy, or

when taken together, Y^1 and Y^2 form:

e) a cyclic boron ester where said chain or ring contains from 2 to 20 carbon atoms, and, optionally, 1, 2, or 3 heteroatoms which can be N, S, or O,

f) a cyclic boron amide where said chain or ring contains from 2 to 20 carbon atoms and, optionally, 1, 2, or 3 heteroatoms which can be N, S, or O,

g) a cyclic boron amide-ester where said chain or ring contains from 2 to 20 carbon atoms and, optionally, 1, 2, or 3 heteroatoms which can be N, S, or O;

R^1 is selected from:

$-CH=CH_2$, $-CH_2CH=CH_2$, $-CH=CHCH_3$,

$-C\equiv CH$, $-C\equiv CCH_3$, $-CH_2C\equiv CH$,

cyclopropyl, $-CH_2$cyclopropyl, cyclobutyl, $-CH_2$cyclobutyl,

-(C_1-C_3 alkyl)SR^{1A}, -CH_2SR^{1A}, -$CH(CH_3)SR^{1A}$, -$CH_2CH_2SR^{1A}$, -$CH_2CH_2CH_2SR^{1A}$, -$CH_2CH(CH_3)SR^{1A}$,

-(C_1-C_3 alkyl)S-SR^{1B}, -CH_2S-SR^{1B}, -CH_2CH_2S-SR^{1B}, -$CH(CH_3)S$-SR^{1B},

-(C_1-C_3 alkyl)S-CO_2R^{1A}, -CH_2S-CO_2R^{1A}, -CH_2CH_2S-CO_2R^{1A},

-(C_1-C_3 alkyl)CO_2R^{1A}, -$CH_2CO_2R^{1A}$, -$CH_2CH_2CO_2R^{1A}$,

C_1-C_4 haloalkyl, -CF_3, -CF_2CF_3, -$CF_2CF_2CF_3$, -$CF_2CF_2CF_2CF_3$, -CF_2CHF_2, -CH_2CHF_2, -CH_2CH_2F, -$CH_2CH_2CF_3$, -$CH_2CH_2CHF_2$, and -$CH_2CH_2CH_2F$;

R^{1A} is H, C_1-C_4 alkyl, phenyl, or -CH_2phenyl, wherein phenyl of R^{1A} is substituted with 0-3 substituents selected from -CH_3, -CF_3, -NO_2, -CN, -OH, -SH, -OCH_3, -OCF_3, -Cl, -Br, -I, and F;

R^{1B} is C_1-C_4 alkyl, phenyl, or -CH_2phenyl, wherein phenyl of R^{1B} is substituted with 0-3 substituents selected from -CH_3, -CF_3, -NO_2, -CN, -OH, -SH, -OCH_3, -OCF_3, -Cl, -Br, -I, and F;

A is a bond, A^1, A^1-A^2, A^1-A^2-A^3, A^1-A^2-A^3-A^4, A^1-A^2-A^3-A^4-A^5, A^1-A^2-A^3-A^4-A^5-A^6, A^1-A^2-A^3-A^4-A^5-A^6-A^7, A^1-A^2-A^3-A^4-A^5-A^6-A^7-A^8, A^1-A^2-A^3-A^4-A^5-A^6-A^7-A^8-A^9; or A^1-A^2-A^3-A^4-A^5-A^6-A^7-A^8-A^9-A^{10};

A^1, A^2, A^3, A^4, A^5, A^6, A^7, A^8, A^9, and A^{10} are independently selected from an amino acid residue, wherein said amino acid residue comprises a natural amino acid, a modified amino acid or an unnatural amino acid;

R^2 is H, C_1-C_4 alkyl, aryl, aryl(C_1-C_4 alkyl)-, or C_3-C_6 cycloalkyl,

R^3 is H, -C(=O)-X-$(CH_2)_m$-Z, C_1-C_4 alkyl, C_2-C_4 alkenyl, C_2-C_4 alkynyl, C_1-C_3 alkyl-R^4, C_2-C_4 alkenyl-R^4,

C_2-C_4 alkynyl-R^4, -C(=O)R^4, -CO_2R^4, -S(=O)R^4, -$S(=O)_2R^4$, -C(=O)NHR^4, aryl, aryl(C_1-C_4 alkyl)-, wherein aryl is optionally substituted with 0-3 substituents selected from -CH_3, -NO_2, -CN, -OH, -OCH_3, -SO_2CH_3, -CF_3, -Cl, -Br, -I, and -F; or an NH_2-blocking group;

R^4 is C_1-C_4 alkyl substituted with 0-1 R^{4A},
C_3-C_6 cycloalkyl substituted with 0-3 R^{4B} and
aryl substituted with 0-3 R^{4B} and
5-14 membered heterocyclic ring system consisting of carbon atoms and 1-4 heteroatoms selected from the group: O, S, and N, and said heterocyclic ring system is substituted with 0-3 R^{4B};

R^{4A} is C_1-C_4 alkyl, halo, -OR^{20}, -SR^{20}, -$NR^{18}R^{19}$,
phenyl substituted with 0-3 R^{4B};
naphthyl substituted with 0-3 R^{4B};
benzyl substituted with 0-3 R^{4B}; or a
5-6 membered heterocyclic ring system containing 1, 2 or 3 heteroatoms selected from nitrogen, oxygen and sulfur; said heterocyclic ring system is substituted with 0-3 R^{4B};

R^{4B} is selected at each occurrence from the group:
H, F, Cl, Br, I, -NO_2, -CN, -NCS, -CF_3, -OCF_3, -CH_3, -CH_2CH_3, -OCH_3, =O, OH, -CO_2H, -SCH_3, -SO_3H, -SO_2CH_3, -NH_2, -$NH(CH_3)$, -$N(CH_3)_2$, phenyl, -CO_2R^{21}, -C(=O)$NR^{21}R^{21}$, -$NHC(=O)R^{21}$, -$NR^{21}R^{21}$, -OR^{21a}, -SR^{21a}, -C(=O)R^{21a}, -S(=O)R^{21a}, -SO_2R^{21}, -$SO_2NR^{21}R^{21}$, C_1-C_4 haloalkyl, C_1-C_4 haloalkoxy, C_1-C_4 thioalkoxy, C_1-C_4 alkyl substituted with 0-3 R^{4C}, C_1-C_4 alkoxy substituted with 0-3 R^{4C}, C_3-C_6 cycloalkyl substituted with 0-3 R^{4C}, aryl substituted with 0-5 R^{4C}, and aryl(C_1-C_4 alkyl)- substituted with 0-5 R^{4C}, and

5-6 membered heterocyclic ring system consisting of carbon atoms and 1-3 heteroatoms selected from the group: O, S, and N, and said heterocyclic ring system is substituted with 0-4 R^{4C};

R^{4C} is selected at each occurrence from the group: H, F, Cl, Br, I, $-NO_2$, -CN, -NCS, $-CF_3$, $-OCF_3$, $-CH_3$, $-OCH_3$, =O, OH, $-CO_2H$, $-SO_2CH_3$, $-NH_2$, $-NH(CH_3)$, $-N(CH_3)_2$, phenyl, $-CO_2R^{21}$, $-C(=O)NR^{21}R^{21}$, $-NHC(=O)R^{21}$, $-NR^{21}R^{21}$, $-OR^{21a}$, $-SR^{21a}$, $-C(=O)R^{21a}$, $-S(=O)R^{21a}$, $-SO_2R^{21}$, $-SO_2NR^{21}R^{21}$, C_1-C_4 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, and C_1-C_4 haloalkoxy;

X is a bond,
C_1-C_4 alkyl substituted with 0-3 R^{11},
C_2-C_4 alkenyl substituted with 0-2 R^{11},
C_3-C_{10} carbocycle substituted with 0-2 R^{11},
C_6-C_{10} aryl substituted with 0-3 R^{11}, or
5-10 membered heterocyclic ring system consisting of carbon atoms and 1-4 heteroatoms selected from the group: O, S, and N, and said heterocyclic ring system is substituted with 0-2 R^{11};

R^{11} at each occurrence is independently selected from H, $-CH_3$, $-CH_2CH_3$, $-NO_2$, $-NH_2$, $-NH(CH_3)$, $-N(CH_3)_2$, $-SO_3H$, $-SO_2CH_3$, $-CO_2H$, $-CF_3$, -OH, $-OCH_3$, $-SCH_3$, $-OCF_3$, -Cl, -Br, -I, -F, =O, -CN, -NCS;
C_2-C_4 alkyl, C_2-C_4 alkoxy, C_2-C_4 thioalkoxy, C_1-C_4 haloalkyl, C_1-C_4 haloalkoxy, $-CO_2R^{21}$, $-C(=O)NR^{21}R^{21}$, $-NHC(=O)R^{21}$, $-NR^{21}R^{11}$, $-OR^{21a}$, $-SR^{21a}$, $-C(=O)R^{21a}$, $-S(=O)R^{21a}$, $-SO_2R^{21}$, $-SO_2NR^{21}R^{21}$, aryl, and aryl(C_1-C_4 alkyl)-, wherein aryl is optionally substituted with 0-3 substituents selected from $-CH_3$, $-NO_2$, -CN, -OH, $-OCH_3$, $-SO_2CH_3$, $-CF_3$, -Cl, -Br, -I, and F;

alternatively, two independent R^{11} groups may optionally be taken together to form $-(CH_2)_p-$;

m is 0, 1, 2, 3, or 4;

p is 1, 2, 3, or 4;

Z is selected from:
-H, $-R^{12}$, -halo, $-NHSO_2R^{12}$, $-SO_2NHR^{12}$, $-SO_2R^{12}$, $-C(=O)R^{12}$, $-OC(=O)C(=O)NHR^{12}$, $-NHC(=O)C(=O)OR^{12}$, $-OC(=O)R^{12}$, $-C(=O)OR^{12}$, $-OR^{12}$, $-SR^{12}$, and -CN;

R^{12} is H,
C_1-C_4 alkyl substituted with 0-3 R^{13},
C_3-C_{10} carbocycle substituted with 0-3 R^{13},
C_6-C_{10} aryl substituted with 0-3 R^{13}, or
5-10 membered heterocyclic ring system consisting of carbon atoms and 1-4 heteroatoms selected from the group: O, S, and N, and said heterocyclic ring system is substituted with 0-3 R^{13};

R^{13} at each occurrence is independently selected from H, $-CH_3$, $-CH_2CH_3$, $-NO_2$, $-SO_2OH$, $-SO_2CH_3$, CF_3, -Cl, -Br, -I, F, $-NH_2$, $-NH(CH_3)$, $-N(CH_3)_2$, $-NH(CH_2CH_3)$, $-N(CH_2CH_3)_2$, and C_1-C_4 alkyl;

R^{18} and R^{19} at each occurrence are independently selected from H, C_1-C_4 alkyl, aryl(C_1-C_4 alkyl)-, and C_3-C_7 cycloalkyl;

R^{20} is C_1-C_4 alkyl;

R^{21} is, at each occurrence, independently H or C_1-C_4 alkyl; and

R^{21a} is, at each occurrence, independently H, C_1-C_4 alkyl, aryl, or C_1-C_4 haloalkyl;

provided when R^1 is $-CH_2CH=CH_2$, then A is not
-Asp-Glu-(2-methyl-Phe)-(3-methyl-Val)-Leu-,
-Asp-Glu-(2-methyl-Phe)-(3-methyl-Val)-(cyclopentyl-Ala)-,
-Asp-Glu-(2-methyl-Phe)-(cyclohexyl-Ala)-Leu-,
-Asp-Glu-(2-methyl-Phe)-(phenyl-Gly)-Leu-,
-Asp-Glu-(2-methyl-Phe)-(cyclohexyl-Ala)-Leu-,
-Asp-Glu-(2-methyl-Phe)-(3-methyl-Val)-(Pro)-,
-Asp-Glu-(2-methyl-Phe)-Phe-Leu-, or
-Asp-Glu-(4-chloro-2-methyl-Phe)-(3-methyl-Val)-(Leu)-.

2. A method of Claim 1 wherein A^1, A^2, A^3, A^4, A^5, A^6, A^7, A^8, A^9, and A^{10} are independently selected from an amino acid residue wherein said amino acid residue comprises a natural amino acid selected from the group: Ala, Arg, Ash, Asp, Aze, Cha, Cys, Dpa, Gln, Glu, Gly, His, Hyp, Ile, Irg, Leu, Lys, Met, Orn, Phe, Phe(4-fluoro), Pro, Sar, Ser, Thr, Trp, Tyr, and Val; a modified amino acid selected from the group: Asp(OMe), Glu(OMe), Hyp(OMe), Asp(O^tBu), Glu(O^tBu), Hyp(O^tBu), Thr(O^tBu), Asp(OBzl), Glu(OBzl), Hyp(OBzl), Thr(OBzl); and an unnatural amino acid.

3. A method of Claim 1 wherein:

A is A^1, A^1-A^2, A^1-A^2-A^3, A^1-A^2-A^3-A^4, A^1-A^2-A^3-A^4-A^5, A^1-A^2-A^3-A^4-A^5-A^6, or A^1-A^2-A^3-A^4-A^5-A^6-A^7; and

A^1, A^2, A^3, A^4, A^5, A^6, and A^7 are independently selected from Ala, Arg, Asn, Asp, Aze, Cha, Cys, Dpa, Gln, Glu, Gly, His, Hyp, Ile, Irg, Leu, Lys, Met, Orn, Phe, Phe(4-fluoro), Pro, Sar, Ser, Thr, Trp, Tyr, Val, Asp(OMe), Glu(OMe), Hyp(OMe), Asp(O^tBu), Glu(O^tBu), Hyp(O^tBu), Thr(O^tBu), Asp(OBzl), Glu(OBzl), Hyp(OBzl), and Thr(OBzl).

4. A method of Claim 3 wherein

Y^1 and Y^2 are independently selected from:

a) -OH,

b) -F,

c) $-NR^{18}R^{19}$,

d) C_1-C_8 alkoxy, or

when taken together, Y^1 and Y^2 form:

e) a cyclic boron ester where said chain or ring contains from 2 to 20 carbon atoms, and, optionally, 1, 2, or 3 heteroatoms which can be N, S, or O,

f) a cyclic boron amide where said chain or ring contains from 2 to 20 carbon atoms and, optionally, 1, 2, or 3 heteroatoms which can be N, S, or O,

g) a cyclic boron amide-ester where said chain or ring contains from 2 to 20 carbon atoms and, optionally, 1, 2, or 3 heteroatoms which can be N, S, or O;

R^1 is selected from:

$-CH=CH_2$, $-CH_2CH=CH_2$, $-CH=CHCH_3$, -cyclopropyl, -cyclopropylmethyl, $-CH_2SR^{1A}$, $-CH_2(CH_3)SR^{1A}$, $-CH_2CO_2R^{1A}$, $-CF_2CF_3$, $-CF_2CF_2CF_3$, $-CH_2CH_2CF_3$, $-CF_2CHF_2$, $-CH_2CHF_2$, $-CH_2CH_2F$, and C_2-C_3 fluoroalkyl;

R^{1A} is H, methyl ,ethyl, propyl, phenyl, or $-CH_2$phenyl, wherein phenyl of R^{1A} is substituted with 0-3 substituents selected from $-CH_3$, $-CF_3$, $-NO_2$, -CN, -OH, -SH, $-OCH_3$, $-OCF_3$, -Cl, -Br, -I, and F;

A is A^1, A^1-A^2, A^1-A^2-A^3, A^1-A^2-A^3-A^4, A^1-A^2-A^3-A^4-A^5, or A^1-A^2-A^3-A^4-A^5-A^6;

A^1, A^2, A^3, A^4, A^5, and A^6 are independently selected from Ala, Arg, Asn, Asp, Aze, Cha, Cys, Dpa, Gln, Glu, Gly, His, Hyp, Ile, Irg, Leu, Lys, Met, Orn, Phe, Phe(4-

fluoro), Pro, Sar, Ser, Thr, Trp, Tyr, Val, Asp(OMe), Glu(OMe), Hyp(OMe), Asp(O^tBu), Glu(O^tBu), Hyp(O^tBu), Thr(O^tBu), Asp(OBzl), Glu(OBzl), Hyp(OBzl), and Thr(OBzl);

R^2 is H, methyl, ethyl, propyl, or butyl;

R^3 is H, $-C(=O)-X-(CH_2)_m-Z$, C_1-C_4 alkyl, C_2-C_4 alkenyl, C_2-C_4 alkynyl, C_1-C_3 alkyl-R^4, C_2-C_4 alkenyl-R^4, C_2-C_4 alkynyl-R^4, $-C(=O)R^4$, $-CO_2R^4$, $-S(=O)R^4$, $-S(=O)_2R^4$, $-C(=O)NHR^4$, aryl, aryl(C_1-C_4 alkyl)-, wherein aryl is optionally substituted with 0-3 substituents selected from $-CH_3$, $-NO_2$, -CN, -OH, $-OCH_3$, $-SO_2CH_3$, $-CF_3$, -Cl, -Br, -I, and -F; or an NH_2-blocking group;

R^4 is C_1-C_4 alkyl substituted with 0-1 R^{4A},
C_3-C_6 cycloalkyl substituted with 0-3 R^{4B} and
aryl substituted with 0-3 R^{4B} and
5-14 membered heterocyclic ring system consisting of carbon atoms and 1-4 heteroatoms selected from the group: O, S, and N, and said heterocyclic ring system is substituted with 0-3 R^{4B};

R^{4A} is C_1-C_4 alkyl, halo, $-OR^{20}$, $-SR^{20}$, $-NR^{18}R^{19}$,
phenyl substituted with 0-3 R^{4B};
naphthyl substituted with 0-3 R^{4B};
benzyl substituted with 0-3 R^{4B}; or a
5-6 membered heterocyclic ring system containing 1, 2 or 3 heteroatoms selected from nitrogen, oxygen and sulfur; said heterocyclic ring system is substituted with 0-3 R^{4B};

R^{4B} is selected at each occurrence from the group:
H, F, Cl, Br, I, $-NO_2$, -CN, -NCS, $-CF_3$, $-OCF_3$, $-CH_3$, $-CH_2CH_3$, $-OCH_3$, =O, OH, $-CO_2H$, $-SCH_3$, $-SO_3H$,

$-SO_2CH_3$, $-NH_2$, $-NH(CH_3)$, $-N(CH_3)_2$, phenyl,
$-CO_2R^{21}$, $-C(=O)NR^{21}R^{21}$, $-NHC(=O)R^{21}$, $-NR^{21}R^{21}$, $-OR^{21a}$,
$-SR^{21a}$, $-C(=O)R^{21a}$, $-S(=O)R^{21a}$, $-SO_2R^{21}$, $-SO_2NR^{21}R^{21}$,
C_1-C_4 haloalkyl, C_1-C_4 haloalkoxy, C_1-C_4 thioalkoxy,
C_1-C_4 alkyl substituted with 0-3 R^{4C},
C_1-C_4 alkoxy substituted with 0-3 R^{4C},
C_3-C_6 cycloalkyl substituted with 0-3 R^{4C},
aryl substituted with 0-5 R^{4C}, and
aryl(C_1-C_4 alkyl)- substituted with 0-5 R^{4C}, and
5-6 membered heterocyclic ring system consisting of carbon atoms and 1-3 heteroatoms selected from the group: O, S, and N, and said heterocyclic ring system is substituted with 0-4 R^{4C};

R^{4C} is selected at each occurrence from the group:
H, F, Cl, Br, I, $-NO_2$, $-CN$, $-NCS$, $-CF_3$, $-OCF_3$,
$-CH_3$, $-OCH_3$, =O, OH, $-CO_2H$, $-SO_2CH_3$, $-NH_2$, $-NH(CH_3)$,
$-N(CH_3)_2$, phenyl, $-CO_2R^{21}$, $-C(=O)NR^{21}R^{21}$, $-NHC(=O)R^{21}$,
$-NR^{21}R^{21}$, $-OR^{21a}$, $-SR^{21a}$, $-C(=O)R^{21a}$, $-S(=O)R^{21a}$,
$-SO_2R^{21}$, $-SO_2NR^{21}R^{21}$, C_1-C_4 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, and C_1-C_4 haloalkoxy;

X is a bond,
C_1-C_4 alkyl substituted with 0-3 R^{11},
C_2-C_4 alkenyl substituted with 0-2 R^{11},
C_3-C_{10} carbocycle substituted with 0-2 R^{11},
C_6-C_{10} aryl substituted with 0-3 R^{11}, or
5-10 membered heterocyclic ring system consisting of carbon atoms and 1-4 heteroatoms selected from the group: O, S, and N, and said heterocyclic ring system is substituted with 0-2 R^{11};

R^{11} at each occurrence is independently selected from
H, $-CH_3$, $-CH_2CH_3$, $-NO_2$, $-NH_2$, $-NH(CH_3)$, $-N(CH_3)_2$,
$-SO_3H$, $-SO_2CH_3$, $-CO_2H$, $-CF_3$, $-OH$, $-OCH_3$, $-SCH_3$, $-OCF_3$,

-Cl, -Br, -I, -F, =O, -CN, -NCS;
C_2-C_4 alkyl, C_2-C_4 alkoxy, C_2-C_4 thioalkoxy,
C_1-C_4 haloalkyl, C_1-C_4 haloalkoxy, $-CO_2R^{21}$,
$-C(=O)NR^{21}R^{21}$, $-NHC(=O)R^{21}$, $-NR^{21}R^{11}$, $-OR^{21a}$, $-SR^{21a}$,
$-C(=O)R^{21a}$, $-S(=O)R^{21a}$, $-SO_2R^{21}$, $-SO_2NR^{21}R^{21}$,
aryl, and aryl(C_1-C_4 alkyl)-, wherein aryl is optionally substituted with 0-3 substituents selected from $-CH_3$, $-NO_2$, -CN, -OH, $-OCH_3$, $-SO_2CH_3$, $-CF_3$, -Cl, -Br, -I, and F;

alternatively, two independent R^{11} groups may optionally be taken together to form $-(CH_2)_p-$;

m is 0, 1, 2, 3, or 4;

p is 1, 2, 3, or 4;

Z is selected from:
-H, $-R^{12}$, -halo, $-NHSO_2R^{12}$, $-SO_2NHR^{12}$, $-SO_2R^{12}$,
$-C(=O)R^{12}$, $-OC(=O)C(=O)NHR^{12}$, $-NHC(=O)C(=O)OR^{12}$,
$-OC(=O)R^{12}$, $-C(=O)OR^{12}$, $-OR^{12}$, $-SR^{12}$, and -CN;

R^{12} is H,
C_1-C_4 alkyl substituted with 0-3 R^{13},
C_3-C_{10} carbocycle substituted with 0-3 R^{13},
C_6-C_{10} aryl substituted with 0-3 R^{13}, or
5-10 membered heterocyclic ring system consisting of carbon atoms and 1-4 heteroatoms selected from the group: O, S, and N, and said heterocyclic ring system is substituted with 0-3 R^{13};

R^{13} at each occurrence is independently selected from H,
$-CH_3$, $-CH_2CH_3$, $-NO_2$, $-SO_2OH$, $-SO_2CH_3$, CF_3, -Cl, -Br,
-I, F, $-NH_2$, $-NH(CH_3)$, $-N(CH_3)_2$, $-NH(CH_2CH_3)$,
$-N(CH_2CH_3)_2$, and C_1-C_4 alkyl;

R^{18} and R^{19} at each occurrence are independently selected from H, C_1-C_4 alkyl, aryl(C_1-C_4 alkyl)-, and C_3-C_7 cycloalkyl;

R^{20} is methyl, ethyl, propyl or butyl;

R^{21} is, at each occurrence, independently H or methyl, ethyl, propyl or butyl; and

R^{21a} is, at each occurrence, independently H, methyl, ethyl, propyl or butyl, phenyl, or C_1-C_4 haloalkyl.

5. A method of Claim 4 wherein

Y^1 and Y^2 are independently selected from:

a) -OH,

b) -F,

c) C_1-C_6 alkoxy, or

when taken together, Y^1 and Y^2 form:

d) a cyclic boron ester where said chain or ring contains from 2 to 16 carbon atoms, and, optionally, 1, 2, or 3 heteroatoms which can be N, S, or O,

R^1 is selected from:

-$CH=CH_2$, -$CH_2CH=CH_2$, -cyclopropyl, -cyclopropylmethyl, -CF_2CF_3, -$CH_2CH_2CF_3$, -CH_2CHF_2, and -CH_2CH_2F,

A is A^1, A^1-A^2, A^1-A^2-A^3, A^1-A^2-A^3-A^4, or A^1-A^2-A^3-A^4-A^5;

A^1, A^2, A^3, and A^4 are independently selected from Ala, Arg, Asn, Asp, Aze, Cha, Cys, Dpa, Gln, Glu, Gly, His, Hyp, Ile, Irg, Leu, Lys, Met, Orn, Phe, Phe(4-fluoro), Pro, Sar, Ser, Thr, Trp, Tyr, Val, Asp(OMe), Glu(OMe), Hyp(OMe), Asp(O^tBu), Glu(O^tBu), Hyp(O^tBu), Thr(O^tBu), Asp(OBzl), Glu(OBzl), Hyp(OBzl), and Thr(OBzl);

R^2 is H, methyl, or ethyl;

R^3 is H, $-C(=O)-X-(CH_2)_m-Z$, C_1-C_4 alkyl, C_2-C_4 alkenyl, C_2-C_4 alkynyl, $-C(=O)R^4$, $-CO_2R^4$, $-S(=O)R^4$, $-S(=O)_2R^4$, $-C(=O)NHR^4$, aryl, aryl(C_1-C_4 alkyl)-, wherein aryl is optionally substituted with 0-3 substituents selected from $-CH_3$, $-NO_2$, -CN, -OH, $-OCH_3$, $-SO_2CH_3$, $-CF_3$, -Cl, -Br, -I, and -F; or an NH_2-blocking group;

R^4 is C_1-C_4 alkyl substituted with 0-1 R^{4A},
C_3-C_6 cycloalkyl substituted with 0-3 R^{4B} and
aryl substituted with 0-3 R^{4B} and
5-14 membered heterocyclic ring system consisting of carbon atoms and 1-4 heteroatoms selected from the group: O, S, and N, and said heterocyclic ring system is substituted with 0-3 R^{4B};

R^{4A} is C_1-C_4 alkyl, halo, $-OR^{20}$, $-SR^{20}$, $-NR^{18}R^{19}$,
phenyl substituted with 0-3 R^{4B};
naphthyl substituted with 0-3 R^{4B};
benzyl substituted with 0-3 R^{4B}; or a
5-6 membered heterocyclic ring system containing 1, 2 or 3 heteroatoms selected from nitrogen, oxygen and sulfur; said heterocyclic ring system is substituted with 0-3 R^{4B};

R^{4B} is selected at each occurrence from the group:
H, F, Cl, Br, I, $-NO_2$, -CN, -NCS, $-CF_3$, $-OCF_3$, $-CH_3$, $-CH_2CH_3$, $-OCH_3$, =O, OH, $-CO_2H$, $-SCH_3$, $-SO_3H$, $-SO_2CH_3$, $-NH_2$, $-NH(CH_3)$, $-N(CH_3)_2$, phenyl, $-CO_2R^{21}$, $-C(=O)NR^{21}R^{21}$, $-NHC(=O)R^{21}$, $-NR^{21}R^{21}$, $-OR^{21a}$, $-SR^{21a}$, $-C(=O)R^{21a}$, $-S(=O)R^{21a}$, $-SO_2R^{21}$, $-SO_2NR^{21}R^{21}$, C_1-C_4 haloalkyl, C_1-C_4 haloalkoxy, C_1-C_4 thioalkoxy, C_1-C_4 alkyl substituted with 0-3 R^{4C}, C_1-C_4 alkoxy substituted with 0-3 R^{4C},

C_3-C_6 cycloalkyl substituted with 0-3 R^{4C},
aryl substituted with 0-5 R^{4C}, and
aryl(C_1-C_4 alkyl)- substituted with 0-5 R^{4C}, and
5-6 membered heterocyclic ring system consisting of carbon atoms and 1-3 heteroatoms selected from the group: O, S, and N, and said heterocyclic ring system is substituted with 0-4 R^{4C};

R^{4C} is selected at each occurrence from the group:
H, F, Cl, Br, I, $-NO_2$, -CN, -NCS, $-CF_3$, $-OCF_3$, $-CH_3$, $-OCH_3$, =O, OH, $-CO_2H$, $-SO_2CH_3$, $-NH_2$, $-NH(CH_3)$, $-N(CH_3)_2$, phenyl, $-CO_2R^{21}$, $-C(=O)NR^{21}R^{21}$, $-NHC(=O)R^{21}$, $-NR^{21}R^{21}$, $-OR^{21a}$, $-SR^{21a}$, $-C(=O)R^{21a}$, $-S(=O)R^{21a}$, $-SO_2R^{21}$, $-SO_2NR^{21}R^{21}$, C_1-C_4 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, and C_1-C_4 haloalkoxy;

X is a bond,
C_1-C_4 alkyl substituted with 0-3 R^{11},
C_2-C_4 alkenyl substituted with 0-2 R^{11},
C_3-C_{10} carbocycle substituted with 0-2 R^{11},
C_6-C_{10} aryl substituted with 0-3 R^{11}, or
5-10 membered heterocyclic ring system consisting of carbon atoms and 1-4 heteroatoms selected from the group: O, S, and N, and said heterocyclic ring system is substituted with 0-2 R^{11};

R^{11} at each occurrence is independently selected from
H, $-CH_3$, $-CH_2CH_3$, $-NO_2$, $-NH_2$, $-NH(CH_3)$, $-N(CH_3)_2$, $-SO_3H$, $-SO_2CH_3$, $-CO_2H$, $-CF_3$, -OH, $-OCH_3$, $-SCH_3$, $-OCF_3$, -Cl, -Br, -I, -F, =O, -CN, -NCS;
C_2-C_4 alkyl, C_2-C_4 alkoxy, C_2-C_4 thioalkoxy,
C_1-C_4 haloalkyl, C_1-C_4 haloalkoxy, $-CO_2R^{21}$,
$-C(=O)NR^{21}R^{21}$, $-NHC(=O)R^{21}$, $-NR^{21}R^{11}$, $-OR^{21a}$, $-SR^{21a}$,
$-C(=O)R^{21a}$, $-S(=O)R^{21a}$, $-SO_2R^{21}$, $-SO_2NR^{21}R^{21}$,

aryl, and aryl(C_1-C_4 alkyl)-, wherein aryl is optionally substituted with 0-3 substituents selected from $-CH_3$, $-NO_2$, -CN, -OH, $-OCH_3$, $-SO_2CH_3$, $-CF_3$, -Cl, -Br, -I, and F;

alternatively, two independent R^{11} groups may optionally be taken together to form $-(CH_2)_p-$;

m is 0, 1, 2, or 3;

p is 1, 2, 3, or 4;

Z is selected from:
-H, $-R^{12}$, -halo, $-NHSO_2R^{12}$, $-SO_2NHR^{12}$, $-SO_2R^{12}$, $-C(=O)R^{12}$, $-OC(=O)C(=O)NHR^{12}$, $-NHC(=O)C(=O)OR^{12}$, $-OC(=O)R^{12}$, $-C(=O)OR^{12}$, $-OR^{12}$, $-SR^{12}$, and -CN;

R^{12} is H,
C_1-C_4 alkyl substituted with 0-3 R^{13},
C_3-C_{10} carbocycle substituted with 0-3 R^{13},
C_6-C_{10} aryl substituted with 0-3 R^{13}, or
5-10 membered heterocyclic ring system consisting of carbon atoms and 1-4 heteroatoms selected from the group: O, S, and N, and said heterocyclic ring system is substituted with 0-3 R^{13};

R^{13} at each occurrence is independently selected from H, $-CH_3$, $-CH_2CH_3$, $-NO_2$, $-SO_2OH$, $-SO_2CH_3$, CF_3, -Cl, -Br, -I, F, $-NH_2$, $-NH(CH_3)$, $-N(CH_3)_2$, $-NH(CH_2CH_3)$, $-N(CH_2CH_3)_2$, and C_1-C_4 alkyl;

R^{18} and R^{19} are independently selected from H, methyl, ethyl, propyl, butyl, benzyl, phenylethyl, cyclopropyl, cyclobutyl, cyclopentyl, and cyclohexyl; and

R^{20} is methyl, ethyl, propyl or butyl;

R^{21} is, at each occurrence, independently H or methyl, ethyl, propyl or butyl; and

R^{21a} is, at each occurrence, independently H, methyl, ethyl, propyl or butyl, phenyl, or C_1-C_4 haloalkyl.

6. A method of Claim 5 wherein

Y^1 and Y^2 are independently selected from:

a) -OH,

b) -F,

b) C_1-C_6 alkoxy, or

when taken together, Y^1 and Y^2 form:

c) a cyclic boron ester where said chain or ring contains from 2 to 12 carbon atoms, and, optionally, 1, 2, or 3 heteroatoms which can be N, S, or O,

R^1 is selected from $-CH_2CH_2CF_3$, $-CH_2CHF_2$, and $-CH_2CH_2F$,

A is A^1-A^2, A^1-A^2-A^3, or A^1-A^2-A^3-A^4;

A^1, A^2, A^3, and A^4 are independently selected from Ala, Arg, Asn, Asp, Aze, Cha, Cys, Dpa, Gln, Glu, Gly, His, Hyp, Ile, Irg, Leu, Lys, Met, Orn, Phe, Phe(4-fluoro), Pro, Sar, Ser, Thr, Trp, Tyr, Val, Asp(OMe), Glu(OMe), Hyp(OMe), Asp(O^tBu), Glu(O^tBu), Hyp(O^tBu), Thr(O^tBu), Asp(OBzl), Glu(OBzl), Hyp(OBzl), and Thr(OBzl);

R^2 is H;

R^3 is H, methyl, ethyl, propyl, butyl, phenyl, benzyl, phenylethyl-, phenylpropyl-, phenylbutyl-, $-C(=O)R^4$, $-S(=O)_2R^4$, $-C(=O)-X-(CH_2)_m-Z$, or an NH_2-blocking group;

R^4 is C_1-C_4 alkyl substituted with 0-1 R^{4A},
C_3-C_6 cycloalkyl substituted with 0-3 R^{4B} and
aryl substituted with 0-2 R^{4B} and
5-10 membered heterocyclic ring system consisting of carbon atoms and 1-4 heteroatoms selected from the group: O, S, and N, and said heterocyclic ring system is substituted with 0-2 R^{4B};

R^{4A} is C_1-C_4 alkyl, halo, $-OR^{20}$, $-SR^{20}$, $-NR^{18}R^{19}$,
phenyl substituted with 0-3 R^{4B};
naphthyl substituted with 0-3 R^{4B};
benzyl substituted with 0-3 R^{4B}; or a
5-6 membered heterocyclic ring system containing 1, 2 or 3 heteroatoms selected from nitrogen, oxygen and sulfur; said heterocyclic ring system is substituted with 0-3 R^{4B};

R^{4B} is selected at each occurrence from the group:
H, F, Cl, Br, I, $-NO_2$, $-CF_3$, $-OCF_3$, $-CH_3$, $-CH_2CH_3$, $-OCH_3$, =O, $-OH$, $-CO_2H$, $-SCH_3$, $-SO_3H$, $-SO_2CH_3$, $-NH_2$, $-NH(CH_3)$, $-N(CH_3)_2$, propyl, butyl, ethoxy, propoxy, butoxy, thioethoxy, thiopropoxy, thiobutoxy, cyclopropyl, cyclobutyl,
phenyl substituted with 0-3 R^{4C};
phenyl(C_1-C_4 alkyl)- substituted with 0-3 R^{4C}, and
5-6 membered heterocyclic ring system consisting of carbon atoms and 1-3 heteroatoms selected from the group: O, S, and N, and said heterocyclic ring system is substituted with 0-3 R^{4C};

R^{4C} is selected at each occurrence from the group:
H, F, Cl, Br, I, $-NO_2$, $-CN$, $-CF_3$, $-OCF_3$, $-CH_3$, $-OCH_3$, OH, and $-SO_2CH_3$;

X is a bond,

C_1-C_4 alkyl substituted with 0-3 R^{11},
C_2-C_4 alkenyl substituted with 0-2 R^{11},
C_3-C_{10} carbocycle substituted with 0-2 R^{11}, wherein the carbocycle is selected from cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, adamantanyl, norbornanyl, norbornenyl, and fluorenyl,
phenyl substituted with 0-3 R^{11},
naphthyl substituted with 0-3 R^{11},
C_5-C_{10} heterocycle substituted with 0-2 R^{11}, wherein the heterocycle is selected from furanyl, oxazolyl, isoxazolyl, benzthiophenyl, pyrrolidinyl, pyrrolyl, carbazolyl, pyridinyl, thiophenyl, triazolyl, thiadiazolyl, benzodioxanyl, benzodioxolyl, quinazolinyl, quinoxalinyl, and quinolinyl;

R^{11} at each occurrence is independently selected from H, $-CH_3$, $-CH_2CH_3$, $-NO_2$, $-NH_2$, $-SO_3H$, $-SO_2CH_3$, $-CO_2H$, $-CF_3$, $-OH$, $-OCH_3$, $-SCH_3$, $-OCF_3$, -Cl, -Br, -I, -F, =O, C_1-C_4 alkyl, C_1-C_4 alkoxy, C_1-C_4 thioalkoxy, phenyl, and phenyl(C_1-C_4 alkyl)-, wherein phenyl is optionally substituted with 0-3 substituents selected from $-CH_3$, $-NO_2$, -CN, -OH, $-OCH_3$, $-OCF_3$, $-SO_2CH_3$, $-CF_3$, -Cl, -Br, -I, and F;

alternatively, two independent R^{11} groups may optionally be taken together to form $-(CH_2)_p-$;

m is 0, 1, or 2;

p is 2, 3, or 4;

Z is selected from:
-H, $-R^{12}$, -halo, $-NHSO_2R^{12}$, $-SO_2NHR^{12}$, $-SO_2R^{12}$, $-C(=O)R^{12}$, $-OC(=O)C(=O)NHR^{12}$, $-NHC(=O)C(=O)OR^{12}$, $-OC(=O)R^{12}$, $-C(=O)OR^{12}$, $-OR^{12}$, $-SR^{12}$, and -CN;

R^{12} is H,
C_1-C_4 alkyl substituted with 0-3 R^{13},
C_3-C_{10} carbocycle substituted with 0-3 R^{13},
phenyl substituted with 0-3 R^{13}, or
C_5-C_{10} heterocycle substituted with 0-3 R^{13}; wherein
the heterocycle is selected from furanyl, oxazolyl, isoxazolyl, pyrrolidinyl, pyrrolyl, pyridinyl, thiophenyl, triazolyl, and thiadiazolyl;

R^{13} at each occurrence is independently selected from H, $-CH_3$, $-CH_2CH_3$, $-NO_2$, $-SO_2OH$, $-SO_2CH_3$, $-CF_3$, -Cl, -Br, -I, -F, $-NH_2$, $-NH(CH_3)$, $-N(CH_3)_2$, $-NH(CH_2CH_3)$, $-N(CH_2CH_3)_2$, methyl, ethyl, propyl, and butyl;

R^{18} and R^{19} are independently selected from H, methyl, ethyl, propyl, butyl, benzyl, phenylethyl, cyclopropyl, cyclobutyl, cyclopentyl, and cyclohexyl; and

R^{20} is methyl, ethyl, propyl or butyl.

7. A method of Claim 5 wherein

Y^1 and Y^2 are independently selected from:
a) -OH,
b) -F,
b) C_1-C_6 alkoxy, or
when taken together, Y^1 and Y^2 form:
c) a cyclic boron ester where said chain or ring contains from 2 to 12 carbon atoms, and, optionally, 1, 2, or 3 heteroatoms which can be N, S, or O,

R^1 is $-CH_2CHF_2$;

A is A^1-A^2, A^1-A^2-A^3, or A^1-A^2-A^3-A^4;

A^1, A^2, A^3, and A^4 are independently selected from Ala, Arg, Asn, Asp, Aze, Cha, Cys, Dpa, Gln, Glu, Gly, His, Hyp, Ile, Irg, Leu, Lys, Met, Orn, Phe, Phe(4-fluoro), Pro, Sar, Ser, Thr, Trp, Tyr, Val, Asp(OMe), Glu(OMe), Hyp(OMe), Asp(O^tBu), Glu(O^tBu), Hyp(O^tBu), Thr(O^tBu), Asp(OBzl), Glu(OBzl), Hyp(OBzl), and Thr(OBzl);

R^2 is H;

R^3 is H, methyl, ethyl, propyl, butyl, phenyl, benzyl, phenylethyl-, phenylpropyl-, phenylbutyl-, $-C(=O)R^4$, $-S(=O)_2R^4$, $-C(=O)-X-(CH_2)_m-Z$, or an NH_2-blocking group;

R^4 is C_1-C_4 alkyl substituted with 0-1 R^{4A},
C_3-C_6 cycloalkyl substituted with 0-3 R^{4B} and
aryl substituted with 0-2 R^{4B} and
5-10 membered heterocyclic ring system consisting of carbon atoms and 1-4 heteroatoms selected from the group: O, S, and N, and said heterocyclic ring system is substituted with 0-2 R^{4B};

R^{4A} is C_1-C_4 alkyl, halo, $-OR^{20}$, $-SR^{20}$, $-NR^{18}R^{19}$,
phenyl substituted with 0-3 R^{4B};
naphthyl substituted with 0-3 R^{4B};
benzyl substituted with 0-3 R^{4B}; or a
5-6 membered heterocyclic ring system containing 1, 2 or 3 heteroatoms selected from nitrogen, oxygen and sulfur; said heterocyclic ring system is substituted with 0-3 R^{4B};

R^{4B} is selected at each occurrence from the group:
H, F, Cl, Br, I, $-NO_2$, $-CF_3$, $-OCF_3$, $-CH_3$, $-CH_2CH_3$, $-OCH_3$, =O, -OH, $-CO_2H$, $-SCH_3$, $-SO_3H$, $-SO_2CH_3$, $-NH_2$,

$-NH(CH_3)$, $-N(CH_3)_2$, propyl, butyl, ethoxy, propoxy, butoxy, thioethoxy, thiopropoxy, thiobutoxy, cyclopropyl, cyclobutyl,
phenyl substituted with 0-3 R^{4C};
phenyl(C_1-C_4 alkyl)- substituted with 0-3 R^{4C}, and
5-6 membered heterocyclic ring system consisting of carbon atoms and 1-3 heteroatoms selected from the group: O, S, and N, and said heterocyclic ring system is substituted with 0-3 R^{4C};

R^{4C} is selected at each occurrence from the group:
H, F, Cl, Br, I, $-NO_2$, -CN, $-CF_3$, $-OCF_3$, $-CH_3$, $-OCH_3$, OH, and $-SO_2CH_3$;

X is a bond,
C_1-C_4 alkyl substituted with 0-3 R^{11},
C_2-C_4 alkenyl substituted with 0-2 R^{11},
C_3-C_{10} carbocycle substituted with 0-2 R^{11}, wherein the carbocycle is selected from cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, adamantanyl, norbornanyl, norbornenyl, and fluorenyl,
phenyl substituted with 0-3 R^{11},
naphthyl substituted with 0-3 R^{11},
C_5-C_{10} heterocycle substituted with 0-2 R^{11}, wherein the heterocycle is selected from furanyl, oxazolyl, isoxazolyl, benzthiophenyl, pyrrolidinyl, pyrrolyl, carbazolyl, pyridinyl, thiophenyl, triazolyl, thiadiazolyl, benzodioxanyl, benzodioxolyl, quinazolinyl, quinoxalinyl, and quinolinyl;

R^{11} at each occurrence is independently selected from H, $-CH_3$, $-CH_2CH_3$, $-NO_2$, $-NH_2$, $-SO_3H$, $-SO_2CH_3$, $-CO_2H$, $-CF_3$, -OH, $-OCH_3$, $-SCH_3$, $-OCF_3$, -Cl, -Br, -I, -F, =O,
C_1-C_4 alkyl, C_1-C_4 alkoxy, C_1-C_4 thioalkoxy, phenyl, and phenyl(C_1-C_4 alkyl)-, wherein phenyl is optionally

substituted with 0-3 substituents selected from $-CH_3$, $-NO_2$, -CN, -OH, $-OCH_3$, $-OCF_3$, $-SO_2CH_3$, $-CF_3$, -Cl, -Br, -I, and F;

alternatively, two independent R^{11} groups may optionally be taken together to form $-(CH_2)_p-$;

m is 0, 1, or 2;

p is 2, 3, or 4;

Z is selected from:
-H, $-R^{12}$, -halo, $-NHSO_2R^{12}$, $-SO_2NHR^{12}$, $-SO_2R^{12}$, $-C(=O)R^{12}$, $-OC(=O)C(=O)NHR^{12}$, $-NHC(=O)C(=O)OR^{12}$, $-OC(=O)R^{12}$, $-C(=O)OR^{12}$, $-OR^{12}$, $-SR^{12}$, and -CN;

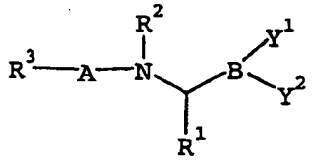
R^{12} is H,
C_1-C_4 alkyl substituted with 0-3 R^{13},
C_3-C_{10} carbocycle substituted with 0-3 R^{13},
phenyl substituted with 0-3 R^{13}, or
C_5-C_{10} heterocycle substituted with 0-3 R^{13}; wherein the heterocycle is selected from furanyl, oxazolyl, isoxazolyl, pyrrolidinyl, pyrrolyl, pyridinyl, thiophenyl, triazolyl, and thiadiazolyl;

R^{13} at each occurrence is independently selected from H, $-CH_3$, $-CH_2CH_3$, $-NO_2$, $-SO_2OH$, $-SO_2CH_3$, $-CF_3$, -Cl, -Br, -I, -F, $-NH_2$, $-NH(CH_3)$, $-N(CH_3)_2$, $-NH(CH_2CH_3)$, $-N(CH_2CH_3)_2$, methyl, ethyl, propyl, and butyl;

R^{18} and R^{19} are independently selected from H, methyl, ethyl, propyl, butyl, benzyl, phenylethyl, cyclopropyl, cyclobutyl, cyclopentyl, and cyclohexyl; and

R^{20} is methyl, ethyl, propyl or butyl.

8. A compound of Formula (I):



(I)

or a pharmaceutically acceptable salt form thereof, wherein:

Y^1 and Y^2 are independently selected from:

a) -OH,

b) -F,

c) $-NR^{18}R^{19}$,

d) C_1-C_8 alkoxy, or

when taken together, Y^1 and Y^2 form:

e) a cyclic boron ester where said chain or ring contains from 2 to 20 carbon atoms, and, optionally, 1, 2, or 3 heteroatoms which can be N, S, or O,

f) a cyclic boron amide where said chain or ring contains from 2 to 20 carbon atoms and, optionally, 1, 2, or 3 heteroatoms which can be N, S, or O,

g) a cyclic boron amide-ester where said chain or ring contains from 2 to 20 carbon atoms and, optionally, 1, 2, or 3 heteroatoms which can be N, S, or O;

R^1 is selected from:

$-CH=CH_2$, $-CH_2CH=CH_2$, $-CH=CHCH_3$, -cyclopropyl, -cyclopropylmethyl, $-CH_2SR^{1A}$, $-CH_2(CH_3)SR^{1A}$, $-CH_2CO_2R^{1A}$, $-CF_2CF_3$, $-CF_2CF_2CF_3$, $-CH_2CH_2CF_3$, $-CF_2CHF_2$, $-CH_2CHF_2$, $-CH_2CH_2F$, and C_2-C_3 fluoroalkyl;

R^{1A} is H, methyl ,ethyl, propyl, phenyl, or $-CH_2$phenyl, wherein phenyl of R^{1A} is substituted with 0-3

substituents selected from $-CH_3$, $-CF_3$, $-NO_2$, -CN, -OH, -SH, $-OCH_3$, $-OCF_3$, -Cl, -Br, -I, and F;

A is A^1, A^1-A^2, A^1-A^2-A^3, A^1-A^2-A^3-A^4, A^1-A^2-A^3-A^4-A^5, or A^1-A^2-A^3-A^4-A^5-A^6;

A^1, A^2, A^3, A^4, A^5, and A^6 are independently selected from Ala, Arg, Asn, Asp, Aze, Cha, Cys, Dpa, Gln, Glu, Gly, His, Hyp, Ile, Irg, Leu, Lys, Met, Orn, Phe, Phe(4-fluoro), Pro, Sar, Ser, Thr, Trp, Tyr, Val, Asp(OMe), Glu(OMe), Hyp(OMe), Asp(O^tBu), Glu(O^tBu), Hyp(O^tBu), Thr(O^tBu), Asp(OBzl), Glu(OBzl), Hyp(OBzl), and Thr(OBzl);

R^2 is H, methyl, ethyl, propyl, or butyl;

R^3 is H, $-C(=O)-X-(CH_2)_m-Z$, C_1-C_4 alkyl, C_2-C_4 alkenyl, C_2-C_4 alkynyl, C_1-C_3 alkyl-R^4, C_2-C_4 alkenyl-R^4, C_2-C_4 alkynyl-R^4, $-C(=O)R^4$, $-CO_2R^4$, $-S(=O)R^4$, $-S(=O)_2R^4$, $-C(=O)NHR^4$, aryl, aryl(C_1-C_4 alkyl)-, wherein aryl is optionally substituted with 0-3 substituents selected from $-CH_3$, $-NO_2$, -CN, -OH, $-OCH_3$, $-SO_2CH_3$, $-CF_3$, -Cl, -Br, -I, and -F; or an NH_2-blocking group;

R^4 is C_1-C_4 alkyl substituted with 0-1 R^{4A},
C_3-C_6 cycloalkyl substituted with 0-3 R^{4B} and
aryl substituted with 0-3 R^{4B} and
5-14 membered heterocyclic ring system consisting of carbon atoms and 1-4 heteroatoms selected from the group: O, S, and N, and said heterocyclic ring system is substituted with 0-3 R^{4B};

R^{4A} is C_1-C_4 alkyl, halo, $-OR^{20}$, $-SR^{20}$, $-NR^{18}R^{19}$,
phenyl substituted with 0-3 R^{4B};
naphthyl substituted with 0-3 R^{4B};

benzyl substituted with 0-3 R^{4B}; or a
5-6 membered heterocyclic ring system containing 1, 2 or 3 heteroatoms selected from nitrogen, oxygen and sulfur; said heterocyclic ring system is substituted with 0-3 R^{4B};

R^{4B} is selected at each occurrence from the group:
H, F, Cl, Br, I, $-NO_2$, -CN, -NCS, $-CF_3$, $-OCF_3$, $-CH_3$, $-CH_2CH_3$, $-OCH_3$, =O, OH, $-CO_2H$, $-SCH_3$, $-SO_3H$, $-SO_2CH_3$, $-NH_2$, $-NH(CH_3)$, $-N(CH_3)_2$, phenyl, $-CO_2R^{21}$, $-C(=O)NR^{21}R^{21}$, $-NHC(=O)R^{21}$, $-NR^{21}R^{21}$, $-OR^{21a}$, $-SR^{21a}$, $-C(=O)R^{21a}$, $-S(=O)R^{21a}$, $-SO_2R^{21}$, $-SO_2NR^{21}R^{21}$, C_1-C_4 haloalkyl, C_1-C_4 haloalkoxy, C_1-C_4 thioalkoxy, C_1-C_4 alkyl substituted with 0-3 R^{4C}, C_1-C_4 alkoxy substituted with 0-3 R^{4C}, C_3-C_6 cycloalkyl substituted with 0-3 R^{4C}, aryl substituted with 0-5 R^{4C}, and aryl(C_1-C_4 alkyl)- substituted with 0-5 R^{4C}, and 5-6 membered heterocyclic ring system consisting of carbon atoms and 1-3 heteroatoms selected from the group: O, S, and N, and said heterocyclic ring system is substituted with 0-4 R^{4C};

R^{4C} is selected at each occurrence from the group:
H, F, Cl, Br, I, $-NO_2$, -CN, -NCS, $-CF_3$, $-OCF_3$, $-CH_3$, $-OCH_3$, =O, OH, $-CO_2H$, $-SO_2CH_3$, $-NH_2$, $-NH(CH_3)$, $-N(CH_3)_2$, phenyl, $-CO_2R^{21}$, $-C(=O)NR^{21}R^{21}$, $-NHC(=O)R^{21}$, $-NR^{21}R^{21}$, $-OR^{21a}$, $-SR^{21a}$, $-C(=O)R^{21a}$, $-S(=O)R^{21a}$, $-SO_2R^{21}$, $-SO_2NR^{21}R^{21}$, C_1-C_4 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, and C_1-C_4 haloalkoxy;

X is a bond,
C_1-C_4 alkyl substituted with 0-3 R^{11},
C_2-C_4 alkenyl substituted with 0-2 R^{11},
C_3-C_{10} carbocycle substituted with 0-2 R^{11},

C_6-C_{10} aryl substituted with 0-3 R^{11}, or
5-10 membered heterocyclic ring system consisting of carbon atoms and 1-4 heteroatoms selected from the group: O, S, and N, and said heterocyclic ring system is substituted with 0-2 R^{11};

R^{11} at each occurrence is independently selected from H, $-CH_3$, $-CH_2CH_3$, $-NO_2$, $-NH_2$, $-NH(CH_3)$, $-N(CH_3)_2$, $-SO_3H$, $-SO_2CH_3$, $-CO_2H$, $-CF_3$, $-OH$, $-OCH_3$, $-SCH_3$, $-OCF_3$, $-Cl$, $-Br$, $-I$, $-F$, $=O$, $-CN$, $-NCS$;
C_2-C_4 alkyl, C_2-C_4 alkoxy, C_2-C_4 thioalkoxy, C_1-C_4 haloalkyl, C_1-C_4 haloalkoxy, $-CO_2R^{21}$, $-C(=O)NR^{21}R^{21}$, $-NHC(=O)R^{21}$, $-NR^{21}R^{11}$, $-OR^{21a}$, $-SR^{21a}$, $-C(=O)R^{21a}$, $-S(=O)R^{21a}$, $-SO_2R^{21}$, $-SO_2NR^{21}R^{21}$, aryl, and aryl(C_1-C_4 alkyl)-, wherein aryl is optionally substituted with 0-3 substituents selected from $-CH_3$, $-NO_2$, $-CN$, $-OH$, $-OCH_3$, $-SO_2CH_3$, $-CF_3$, $-Cl$, -Br, $-I$, and F;

alternatively, two independent R^{11} groups may optionally be taken together to form $-(CH_2)_p-$;

m is 0, 1, 2, 3, or 4;

p is 1, 2, 3, or 4;

Z is selected from:
-H, $-R^{12}$, -halo, $-NHSO_2R^{12}$, $-SO_2NHR^{12}$, $-SO_2R^{12}$, $-C(=O)R^{12}$, $-OC(=O)C(=O)NHR^{12}$, $-NHC(=O)C(=O)OR^{12}$, $-OC(=O)R^{12}$, $-C(=O)OR^{12}$, $-OR^{12}$, $-SR^{12}$, and $-CN$;

R^{12} is H,
C_1-C_4 alkyl substituted with 0-3 R^{13},
C_3-C_{10} carbocycle substituted with 0-3 R^{13},
C_6-C_{10} aryl substituted with 0-3 R^{13}, or

5-10 membered heterocyclic ring system consisting of carbon atoms and 1-4 heteroatoms selected from the group: O, S, and N, and said heterocyclic ring system is substituted with 0-3 R^{13};

R^{13} at each occurrence is independently selected from H, $-CH_3$, $-CH_2CH_3$, $-NO_2$, $-SO_2OH$, $-SO_2CH_3$, CF_3, -Cl, -Br, -I, F, $-NH_2$, $-NH(CH_3)$, $-N(CH_3)_2$, $-NH(CH_2CH_3)$, $-N(CH_2CH_3)_2$, and C_1-C_4 alkyl;

R^{18} and R^{19} at each occurrence are independently selected from H, C_1-C_4 alkyl, aryl(C_1-C_4 alkyl)-, and C_3-C_7 cycloalkyl;

R^{20} is methyl, ethyl, propyl or butyl;

R^{21} is, at each occurrence, independently H or methyl, ethyl, propyl or butyl; and

R^{21a} is, at each occurrence, independently H, methyl, ethyl, propyl or butyl, phenyl, or C_1-C_4 haloalkyl;

provided when R^1 is $-CH_2CH_2F$, the A is not -Gly-Pro-;
provided when R^1 is $-CH_2CH=CH_2$, then A is not
-Asp-Glu-(2-methyl-Phe)-(3-methyl-Val)-Leu-,
-Asp-Glu-(2-methyl-Phe)-(3-methyl-Val)-(cyclopentyl-Ala)-,
-Asp-Glu-(2-methyl-Phe)-(cyclohexyl-Ala)-Leu-,
-Asp-Glu-(2-methyl-Phe)-(phenyl-Gly)-Leu-,
-Asp-Glu-(2-methyl-Phe)-(cyclohexyl-Ala)-Leu-,
-Asp-Glu-(2-methyl-Phe)-(3-methyl-Val)-(Pro)-,
-Asp-Glu-(2-methyl-Phe)-Phe-Leu-, or
-Asp-Glu-(4-chloro-2-methyl-Phe)-(3-methyl-Val)-(Leu)-.

9. A compound of Claim 8 wherein

Y^1 and Y^2 are independently selected from:

a) -OH,
b) -F,
c) C_1-C_6 alkoxy, or

when taken together, Y^1 and Y^2 form:

d) a cyclic boron ester where said chain or ring contains from 2 to 16 carbon atoms, and, optionally, 1, 2, or 3 heteroatoms which can be N, S, or O,

R^1 is selected from:
$-CH=CH_2$, $-CH_2CH=CH_2$, -cyclopropyl, -cyclopropylmethyl, $-CF_2CF_3$, $-CH_2CH_2CF_3$, $-CH_2CHF_2$, and $-CH_2CH_2F$,

A is A^1, A^1-A^2, A^1-A^2-A^3, A^1-A^2-A^3-A^4, or A^1-A^2-A^3-A^4-A^5;

A^1, A^2, A^3, and A^4 are independently selected from Ala, Arg, Asn, Asp, Aze, Cha, Cys, Dpa, Gln, Glu, Gly, His, Hyp, Ile, Irg, Leu, Lys, Met, Orn, Phe, Phe(4-fluoro), Pro, Sar, Ser, Thr, Trp, Tyr, Val, Asp(OMe), Glu(OMe), Hyp(OMe), Asp(O^tBu), Glu(O^tBu), Hyp(O^tBu), Thr(O^tBu), Asp(OBzl), Glu(OBzl), Hyp(OBzl), and Thr(OBzl);

R^2 is H, methyl, or ethyl;

R^3 is H, $-C(=O)-X-(CH_2)_m-Z$, C_1-C_4 alkyl, C_2-C_4 alkenyl, C_2-C_4 alkynyl, $-C(=O)R^4$, $-CO_2R^4$, $-S(=O)R^4$, $-S(=O)_2R^4$, $-C(=O)NHR^4$, aryl, aryl(C_1-C_4 alkyl)-, wherein aryl is optionally substituted with 0-3 substituents selected from $-CH_3$, $-NO_2$, -CN, -OH, $-OCH_3$, $-SO_2CH_3$, $-CF_3$, -Cl, -Br, -I, and -F; or an NH_2-blocking group;

R^4 is C_1-C_4 alkyl substituted with 0-1 R^{4A},
C_3-C_6 cycloalkyl substituted with 0-3 R^{4B} and
aryl substituted with 0-3 R^{4B} and
5-14 membered heterocyclic ring system consisting of carbon atoms and 1-4 heteroatoms selected from

the group: O, S, and N, and said heterocyclic ring system is substituted with 0-3 R^{4B};

R^{4A} is C_1-C_4 alkyl, halo, $-OR^{20}$, $-SR^{20}$, $-NR^{18}R^{19}$,
phenyl substituted with 0-3 R^{4B};
naphthyl substituted with 0-3 R^{4B};
benzyl substituted with 0-3 R^{4B}; or a
5-6 membered heterocyclic ring system containing 1, 2 or 3 heteroatoms selected from nitrogen, oxygen and sulfur; said heterocyclic ring system is substituted with 0-3 R^{4B};

R^{4B} is selected at each occurrence from the group:
H, F, Cl, Br, I, $-NO_2$, -CN, -NCS, $-CF_3$, $-OCF_3$, $-CH_3$, $-CH_2CH_3$, $-OCH_3$, =O, OH, $-CO_2H$, $-SCH_3$, $-SO_3H$, $-SO_2CH_3$, $-NH_2$, $-NH(CH_3)$, $-N(CH_3)_2$, phenyl, $-CO_2R^{21}$, $-C(=O)NR^{21}R^{21}$, $-NHC(=O)R^{21}$, $-NR^{21}R^{21}$, $-OR^{21a}$, $-SR^{21a}$, $-C(=O)R^{21a}$, $-S(=O)R^{21a}$, $-SO_2R^{21}$, $-SO_2NR^{21}R^{21}$, C_1-C_4 haloalkyl, C_1-C_4 haloalkoxy, C_1-C_4 thioalkoxy, C_1-C_4 alkyl substituted with 0-3 R^{4C}, C_1-C_4 alkoxy substituted with 0-3 R^{4C}, C_3-C_6 cycloalkyl substituted with 0-3 R^{4C}, aryl substituted with 0-5 R^{4C}, and aryl(C_1-C_4 alkyl)- substituted with 0-5 R^{4C}, and
5-6 membered heterocyclic ring system consisting of carbon atoms and 1-3 heteroatoms selected from the group: O, S, and N, and said heterocyclic ring system is substituted with 0-4 R^{4C};

R^{4C} is selected at each occurrence from the group:
H, F, Cl, Br, I, $-NO_2$, -CN, -NCS, $-CF_3$, $-OCF_3$, $-CH_3$, $-OCH_3$, =O, OH, $-CO_2H$, $-SO_2CH_3$, $-NH_2$, $-NH(CH_3)$, $-N(CH_3)_2$, phenyl, $-CO_2R^{21}$, $-C(=O)NR^{21}R^{21}$, $-NHC(=O)R^{21}$, $-NR^{21}R^{21}$, $-OR^{21a}$, $-SR^{21a}$, $-C(=O)R^{21a}$, $-S(=O)R^{21a}$,

$-SO_2R^{21}$, $-SO_2NR^{21}R^{21}$, C_1-C_4 alkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkyl, and C_1-C_4 haloalkoxy;

X is a bond,
C_1-C_4 alkyl substituted with 0-3 R^{11},
C_2-C_4 alkenyl substituted with 0-2 R^{11},
C_3-C_{10} carbocycle substituted with 0-2 R^{11},
C_6-C_{10} aryl substituted with 0-3 R^{11}, or
5-10 membered heterocyclic ring system consisting of carbon atoms and 1-4 heteroatoms selected from the group: O, S, and N, and said heterocyclic ring system is substituted with 0-2 R^{11};

R^{11} at each occurrence is independently selected from
H, $-CH_3$, $-CH_2CH_3$, $-NO_2$, $-NH_2$, $-NH(CH_3)$, $-N(CH_3)_2$, $-SO_3H$, $-SO_2CH_3$, $-CO_2H$, $-CF_3$, $-OH$, $-OCH_3$, $-SCH_3$, $-OCF_3$, $-Cl$, $-Br$, $-I$, $-F$, $=O$, $-CN$, $-NCS$;
C_2-C_4 alkyl, C_2-C_4 alkoxy, C_2-C_4 thioalkoxy, C_1-C_4 haloalkyl, C_1-C_4 haloalkoxy, $-CO_2R^{21}$, $-C(=O)NR^{21}R^{21}$, $-NHC(=O)R^{21}$, $-NR^{21}R^{11}$, $-OR^{21a}$, $-SR^{21a}$, $-C(=O)R^{21a}$, $-S(=O)R^{21a}$, $-SO_2R^{21}$, $-SO_2NR^{21}R^{21}$,
aryl, and aryl(C_1-C_4 alkyl)-, wherein aryl is optionally substituted with 0-3 substituents selected from $-CH_3$, $-NO_2$, $-CN$, $-OH$, $-OCH_3$, $-SO_2CH_3$, $-CF_3$, $-Cl$, -Br, -I, and F;

alternatively, two independent R^{11} groups may optionally be taken together to form $-(CH_2)_p-$;

m is 0, 1, 2, or 3;

p is 1, 2, 3, or 4;

Z is selected from:
$-H$, $-R^{12}$, -halo, $-NHSO_2R^{12}$, $-SO_2NHR^{12}$, $-SO_2R^{12}$,

$-C(=O)R^{12}$, $-OC(=O)C(=O)NHR^{12}$, $-NHC(=O)C(=O)OR^{12}$, $-OC(=O)R^{12}$, $-C(=O)OR^{12}$, $-OR^{12}$, $-SR^{12}$, and $-CN$;

R^{12} is H,
C_1-C_4 alkyl substituted with 0-3 R^{13},
C_3-C_{10} carbocycle substituted with 0-3 R^{13},
C_6-C_{10} aryl substituted with 0-3 R^{13}, or
5-10 membered heterocyclic ring system consisting of carbon atoms and 1-4 heteroatoms selected from the group: O, S, and N, and said heterocyclic ring system is substituted with 0-3 R^{13};

R^{13} at each occurrence is independently selected from H, $-CH_3$, $-CH_2CH_3$, $-NO_2$, $-SO_2OH$, $-SO_2CH_3$, CF_3, -Cl, -Br, -I, F, $-NH_2$, $-NH(CH_3)$, $-N(CH_3)_2$, $-NH(CH_2CH_3)$, $-N(CH_2CH_3)_2$, and C_1-C_4 alkyl;

R^{18} and R^{19} are independently selected from H, methyl, ethyl, propyl, butyl, benzyl, phenylethyl, cyclopropyl, cyclobutyl, cyclopentyl, and cyclohexyl; and

R^{20} is methyl, ethyl, propyl or butyl;

R^{21} is, at each occurrence, independently H or methyl, ethyl, propyl or butyl; and

R^{21a} is, at each occurrence, independently H, methyl, ethyl, propyl or butyl, phenyl, or C_1-C_4 haloalkyl.

10. A compound of Claim 9 wherein

Y^1 and Y^2 are independently selected from:
a) -OH,
b) -F,
b) C_1-C_6 alkoxy, or

when taken together, Y^1 and Y^2 form:

c) a cyclic boron ester where said chain or ring contains from 2 to 12 carbon atoms, and, optionally, 1, 2, or 3 heteroatoms which can be N, S, or O,

R^1 is selected from $-CH_2CH_2CF_3$, $-CH_2CHF_2$, and $-CH_2CH_2F$,

A is A^1-A^2, A^1-A^2-A^3, or A^1-A^2-A^3-A^4;

A^1, A^2, A^3, and A^4 are independently selected from Ala, Arg, Asn, Asp, Aze, Cha, Cys, Dpa, Gln, Glu, Gly, His, Hyp, Ile, Irg, Leu, Lys, Met, Orn, Phe, Phe(4-fluoro), Pro, Sar, Ser, Thr, Trp, Tyr, Val, Asp(OMe), Glu(OMe), Hyp(OMe), Asp(O^tBu), Glu(O^tBu), Hyp(O^tBu), Thr(O^tBu), Asp(OBzl), Glu(OBzl), Hyp(OBzl), and Thr(OBzl);

R^2 is H;

R^3 is H, methyl, ethyl, propyl, butyl, phenyl, benzyl, phenylethyl-, phenylpropyl-, phenylbutyl-, $-C(=O)R^4$, $-S(=O)_2R^4$, $-C(=O)-X-(CH_2)_m-Z$, or an NH_2-blocking group;

R^4 is C_1-C_4 alkyl substituted with 0-1 R^{4A},
C_3-C_6 cycloalkyl substituted with 0-3 R^{4B} and
aryl substituted with 0-2 R^{4B} and
5-10 membered heterocyclic ring system consisting of carbon atoms and 1-4 heteroatoms selected from the group: O, S, and N, and said heterocyclic ring system is substituted with 0-2 R^{4B};

R^{4A} is C_1-C_4 alkyl, halo, $-OR^{20}$, $-SR^{20}$, $-NR^{18}R^{19}$,
phenyl substituted with 0-3 R^{4B};
naphthyl substituted with 0-3 R^{4B};
benzyl substituted with 0-3 R^{4B}; or a

5-6 membered heterocyclic ring system containing 1, 2 or 3 heteroatoms selected from nitrogen, oxygen and sulfur; said heterocyclic ring system is substituted with 0-3 R^{4B};

R^{4B} is selected at each occurrence from the group:
H, F, Cl, Br, I, $-NO_2$, $-CF_3$, $-OCF_3$, $-CH_3$, $-CH_2CH_3$, $-OCH_3$, =O, -OH, $-CO_2H$, $-SCH_3$, $-SO_3H$, $-SO_2CH_3$, $-NH_2$, $-NH(CH_3)$, $-N(CH_3)_2$, propyl, butyl, ethoxy, propoxy, butoxy, thioethoxy, thiopropoxy, thiobutoxy, cyclopropyl, cyclobutyl,
phenyl substituted with 0-3 R^{4C};
phenyl(C_1-C_4 alkyl)- substituted with 0-3 R^{4C}, and
5-6 membered heterocyclic ring system consisting of carbon atoms and 1-3 heteroatoms selected from the group: O, S, and N, and said heterocyclic ring system is substituted with 0-3 R^{4C};

R^{4C} is selected at each occurrence from the group:
H, F, Cl, Br, I, $-NO_2$, -CN, $-CF_3$, $-OCF_3$, $-CH_3$, $-OCH_3$, OH, and $-SO_2CH_3$;

X is a bond,
C_1-C_4 alkyl substituted with 0-3 R^{11},
C_2-C_4 alkenyl substituted with 0-2 R^{11},
C_3-C_{10} carbocycle substituted with 0-2 R^{11}, wherein the carbocycle is selected from cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, adamantanyl, norbornanyl, norbornenyl, and fluorenyl,
phenyl substituted with 0-3 R^{11},
naphthyl substituted with 0-3 R^{11},
C_5-C_{10} heterocycle substituted with 0-2 R^{11}, wherein the heterocycle is selected from furanyl, oxazolyl, isoxazolyl, benzthiophenyl, pyrrolidinyl, pyrrolyl, carbazolyl, pyridinyl, thiophenyl, triazolyl, thiadiazolyl,

benzodioxanyl, benzodioxolyl, quinazolinyl, quinoxalinyl, and quinolinyl;

R^{11} at each occurrence is independently selected from H, $-CH_3$, $-CH_2CH_3$, $-NO_2$, $-NH_2$, $-SO_3H$, $-SO_2CH_3$, $-CO_2H$, $-CF_3$, $-OH$, $-OCH_3$, $-SCH_3$, $-OCF_3$, $-Cl$, $-Br$, $-I$, $-F$, $=O$, C_1-C_4 alkyl, C_1-C_4 alkoxy, C_1-C_4 thioalkoxy, phenyl, and phenyl(C_1-C_4 alkyl)-, wherein phenyl is optionally substituted with 0-3 substituents selected from $-CH_3$, $-NO_2$, $-CN$, $-OH$, $-OCH_3$, $-OCF_3$, $-SO_2CH_3$, $-CF_3$, $-Cl$, $-Br$, $-I$, and F;

alternatively, two independent R^{11} groups may optionally be taken together to form $-(CH_2)_p-$;

m is 0, 1, or 2;

p is 2, 3, or 4;

Z is selected from:
$-H$, $-R^{12}$, -halo, $-NHSO_2R^{12}$, $-SO_2NHR^{12}$, $-SO_2R^{12}$, $-C(=O)R^{12}$, $-OC(=O)C(=O)NHR^{12}$, $-NHC(=O)C(=O)OR^{12}$, $-OC(=O)R^{12}$, $-C(=O)OR^{12}$, $-OR^{12}$, $-SR^{12}$, and $-CN$;

R^{12} is H,
C_1-C_4 alkyl substituted with 0-3 R^{13},
C_3-C_{10} carbocycle substituted with 0-3 R^{13},
phenyl substituted with 0-3 R^{13}, or
C_5-C_{10} heterocycle substituted with 0-3 R^{13}; wherein the heterocycle is selected from furanyl, oxazolyl, isoxazolyl, pyrrolidinyl, pyrrolyl, pyridinyl, thiophenyl, triazolyl, and thiadiazolyl;

R^{13} at each occurrence is independently selected from H,

$-CH_3$, $-CH_2CH_3$, $-NO_2$, $-SO_2OH$, $-SO_2CH_3$, $-CF_3$, -Cl, -Br, -I, -F, $-NH_2$, $-NH(CH_3)$, $-N(CH_3)_2$, $-NH(CH_2CH_3)$, $-N(CH_2CH_3)_2$, methyl, ethyl, propyl, and butyl;

R^{18} and R^{19} are independently selected from H, methyl, ethyl, propyl, butyl, benzyl, phenylethyl, cyclopropyl, cyclobutyl, cyclopentyl, and cyclohexyl; and

R^{20} is methyl, ethyl, propyl or butyl.

11. A compound of Claim 9 wherein

Y^1 and Y^2 are independently selected from:

a) -OH,

b) -F,

b) C_1-C_6 alkoxy, or

when taken together, Y^1 and Y^2 form:

c) a cyclic boron ester where said chain or ring contains from 2 to 12 carbon atoms, and, optionally, 1, 2, or 3 heteroatoms which can be N, S, or O,

R^1 is $-CH_2CHF_2$;

A is A^1-A^2, A^1-A^2-A^3, or A^1-A^2-A^3-A^4;

A^1, A^2, A^3, and A^4 are independently selected from Ala, Arg, Asn, Asp, Aze, Cha, Cys, Dpa, Gln, Glu, Gly, His, Hyp, Ile, Irg, Leu, Lys, Met, Orn, Phe, Phe(4-fluoro), Pro, Sar, Ser, Thr, Trp, Tyr, Val, Asp(OMe), Glu(OMe), Hyp(OMe), Asp(O^tBu), Glu(O^tBu), Hyp(O^tBu), Thr(O^tBu), Asp(OBzl), Glu(OBzl), Hyp(OBzl), and Thr(OBzl);

R^2 is H;

R^3 is H, methyl, ethyl, propyl, butyl, phenyl, benzyl, phenylethyl-, phenylpropyl-, phenylbutyl-, $-C(=O)R^4$, $-S(=O)_2R^4$, $-C(=O)-X-(CH_2)_m-Z$, or an NH_2-blocking group;

R^4 is C_1-C_4 alkyl substituted with 0-1 R^{4A},
C_3-C_6 cycloalkyl substituted with 0-3 R^{4B} and
aryl substituted with 0-2 R^{4B} and
5-10 membered heterocyclic ring system consisting of carbon atoms and 1-4 heteroatoms selected from the group: O, S, and N, and said heterocyclic ring system is substituted with 0-2 R^{4B};

R^{4A} is C_1-C_4 alkyl, halo, $-OR^{20}$, $-SR^{20}$, $-NR^{18}R^{19}$,
phenyl substituted with 0-3 R^{4B};
naphthyl substituted with 0-3 R^{4B};
benzyl substituted with 0-3 R^{4B}; or a
5-6 membered heterocyclic ring system containing 1, 2 or 3 heteroatoms selected from nitrogen, oxygen and sulfur; said heterocyclic ring system is substituted with 0-3 R^{4B};

R^{4B} is selected at each occurrence from the group:
H, F, Cl, Br, I, $-NO_2$, $-CF_3$, $-OCF_3$, $-CH_3$, $-CH_2CH_3$, $-OCH_3$, =O, -OH, $-CO_2H$, $-SCH_3$, $-SO_3H$, $-SO_2CH_3$, $-NH_2$, $-NH(CH_3)$, $-N(CH_3)_2$, propyl, butyl, ethoxy, propoxy, butoxy, thioethoxy, thiopropoxy, thiobutoxy, cyclopropyl, cyclobutyl,
phenyl substituted with 0-3 R^{4C};
phenyl(C_1-C_4 alkyl)- substituted with 0-3 R^{4C}, and
5-6 membered heterocyclic ring system consisting of carbon atoms and 1-3 heteroatoms selected from the group: O, S, and N, and said heterocyclic ring system is substituted with 0-3 R^{4C};

R^{4C} is selected at each occurrence from the group:

H, F, Cl, Br, I, $-NO_2$, -CN, $-CF_3$, $-OCF_3$, $-CH_3$, $-OCH_3$, OH, and $-SO_2CH_3$;

X is a bond,

C_1-C_4 alkyl substituted with 0-3 R^{11},

C_2-C_4 alkenyl substituted with 0-2 R^{11},

C_3-C_{10} carbocycle substituted with 0-2 R^{11}, wherein the carbocycle is selected from cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, adamantanyl, norbornanyl, norbornenyl, and fluorenyl,

phenyl substituted with 0-3 R^{11},

naphthyl substituted with 0-3 R^{11},

C_5-C_{10} heterocycle substituted with 0-2 R^{11}, wherein the heterocycle is selected from furanyl, oxazolyl, isoxazolyl, benzthiophenyl, pyrrolidinyl, pyrrolyl, carbazolyl, pyridinyl, thiophenyl, triazolyl, thiadiazolyl, benzodioxanyl, benzodioxolyl, quinazolinyl, quinoxalinyl, and quinolinyl;

R^{11} at each occurrence is independently selected from H, $-CH_3$, $-CH_2CH_3$, $-NO_2$, $-NH_2$, $-SO_3H$, $-SO_2CH_3$, $-CO_2H$, $-CF_3$, -OH, $-OCH_3$, $-SCH_3$, $-OCF_3$, -Cl, -Br, -I, -F, =O, C_1-C_4 alkyl, C_1-C_4 alkoxy, C_1-C_4 thioalkoxy, phenyl, and phenyl(C_1-C_4 alkyl)-, wherein phenyl is optionally substituted with 0-3 substituents selected from $-CH_3$, $-NO_2$, -CN, -OH, $-OCH_3$, $-OCF_3$, $-SO_2CH_3$, $-CF_3$, -Cl, -Br, -I, and F;

alternatively, two independent R^{11} groups may optionally be taken together to form $-(CH_2)_p-$;

m is 0, 1, or 2;

p is 2, 3, or 4;

Z is selected from:

-H, -R^{12}, -halo, -$NHSO_2R^{12}$, -SO_2NHR^{12}, -SO_2R^{12}, -$C(=O)R^{12}$, -$OC(=O)C(=O)NHR^{12}$, -$NHC(=O)C(=O)OR^{12}$, -$OC(=O)R^{12}$, -$C(=O)OR^{12}$, -OR^{12}, -SR^{12}, and -CN;

R^{12} is H,

C_1-C_4 alkyl substituted with 0-3 R^{13},

C_3-C_{10} carbocycle substituted with 0-3 R^{13},

phenyl substituted with 0-3 R^{13}, or

C_5-C_{10} heterocycle substituted with 0-3 R^{13}; wherein the heterocycle is selected from furanyl, oxazolyl, isoxazolyl, pyrrolidinyl, pyrrolyl, pyridinyl, thiophenyl, triazolyl, and thiadiazolyl;

R^{13} at each occurrence is independently selected from H, -CH_3, -CH_2CH_3, -NO_2, -SO_2OH, -SO_2CH_3, -CF_3, -Cl, -Br, -I, -F, -NH_2, -$NH(CH_3)$, -$N(CH_3)_2$, -$NH(CH_2CH_3)$, -$N(CH_2CH_3)_2$, methyl, ethyl, propyl, and butyl;

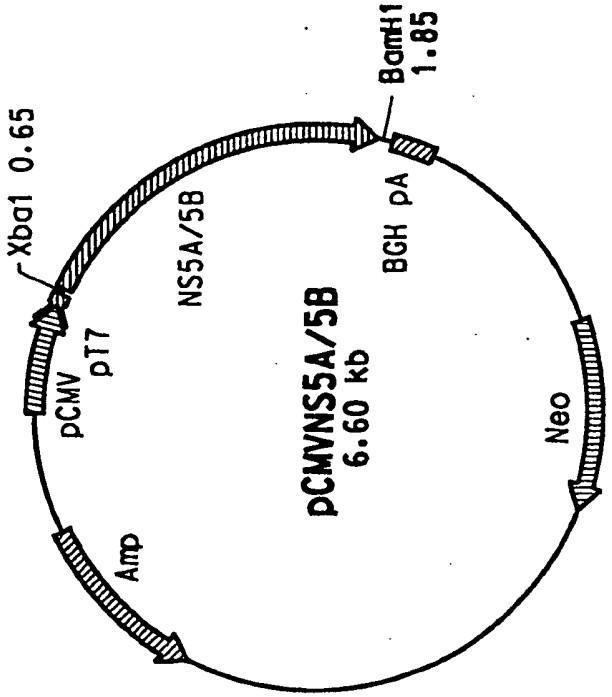
R^{18} and R^{19} are independently selected from H, methyl, ethyl, propyl, butyl, benzyl, phenylethyl, cyclopropyl, cyclobutyl, cyclopentyl, and cyclohexyl; and

R^{20} is methyl, ethyl, propyl or butyl.

12. A compound selected from Examples 7-17, 19-22, 27-41, 43-53, 54a-54f, 59a-59bj, and 60a-60bc.

13. A pharmaceutical composition comprising a compound according to one of Claims 8-11 and a pharmaceutically acceptable carrier.

14. A pharmaceutical composition comprising a compound of Claim 12 and a pharmaceutically acceptable carrier.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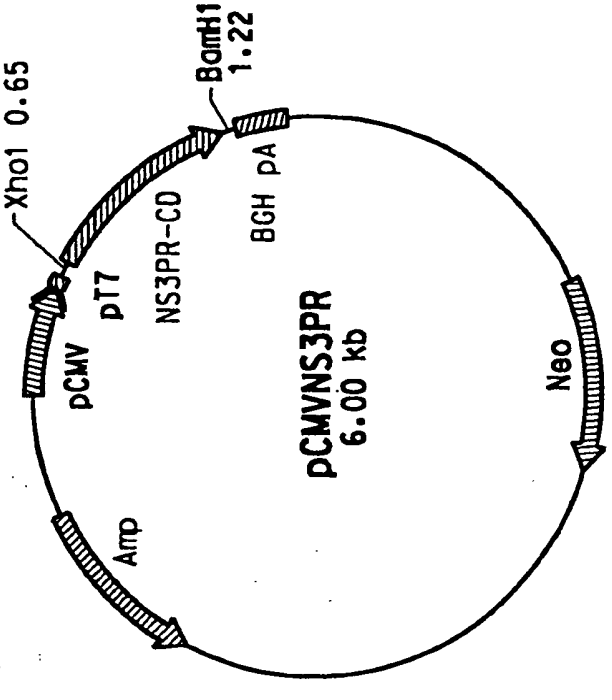
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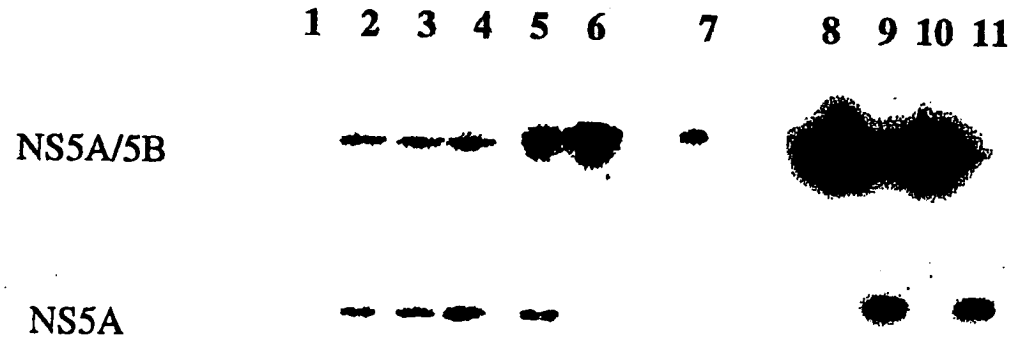
FIG. 1

FIG. 2



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7. NS5A/B Control
8. NS5A/B xf
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10. NS3 mut +NS5A/B co-xf
11. NS3/4+NS5A/B co-xf

SEQUENCE LISTING

<110> KETTNER, CHARLES
Jagannathan, Sharada
Forsyth, Timothy
DuPont Pharmaceuticals Company

<120> Peptide Boronic Acid Inhibitors of Hepatitis C Virus Protease

<130> DM-7021 HCV Sequence ID listing

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<220>
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<400> 9
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1 5

<210> 10
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5